

Another Whiff of Doomsday

THE latest contribution to this rich season of sombre speculation about the future—or the danger that there will be no future—also happens to be the first pronouncement of the organization set up four years ago by Dr Aurelio Peccei to study “The Predicament of Mankind”, and which has since become known as the Club of Rome. The introduction to this document, published this week in the United States (*The Limits to Growth*, Potomac Associates, \$2.75), says that the members of the club are united “by their overriding conviction that the major problems facing mankind are of such complexity and are so interrelated that traditional institutions and policies are no longer able to cope with them nor able to come to grips with their full content”.

The text itself is not as original as might have been expected. Much of it is derived by simplification from Professor J. W. Forrester's *World Dynamics* (Cambridge, Mass., 1971), itself a somewhat dangerously over-simple document. Inevitably, however, *The Limits to Growth* is likely to spark off yet another wave of public anxiety about the decades which lie ahead, and indeed there is a good chance that the product of what is described as the “MIT team” will emerge as the most influential contribution so far to the literature of Doomsday. In the circumstances, it is proper to acknowledge in advance that the book will probably also become a focus for controversy, for there are the seeds of fierce arguments in its assumptions and its conclusions. On balance, in spite of its provenance, the book is at once over-simple and confusing.

Like Malthus and his recent disciples, Dr Paul Ehrlich for example, Dr Dennis L. Meadows and his co-authors begin with the simple truth that continued exponential growth of any numerical attribute of society is impossible. This, of course, is beyond dispute. If the population of the world appears to be increasing exponentially, or if its consumption of iron ore or its production of disposable bottles seems to be increasing exponentially, it requires no flair for prophecy but merely a simple understanding of the differential calculus to know that exponential growth will sooner or later be replaced by some other and more moderate law of growth. The interest of prophecy in matters like these lies in the extent to which it may be possible to guess how exponential growth will at some stage be attenuated.

In this sense, it will be observed, even the great Malthus (at least in the first edition of his *Essay*) was not so much a prophet as a commentator on the algebraic properties of exponential functions. He urged that if the population of Britain continued to grow “geometrically”, the time would come when famine and pestilence would supervene. The alternative, he said, was that the British population should exercise “moral restraint” in reproduction. Malthus was, in other words, not so much a prophet as an admonitory figure, urging his compatriots to a change of habit that would help somehow to ensure survival.

In spite of the MIT connexions of Dr Meadows and his

team, and the impressive use of computer simulation of the course of future events with which the book is provided, the Club of Rome's first study is in this same evangelical mould. As the club's executive committee says in its endorsement of the study, “any deliberate attempt to reach a rational and enduring state of equilibrium by planned measures rather than by chance or catastrophe must ultimately be founded on a basic change of values and goals at individual, national and world levels”. REPENT, OR THE END OF THE WORLD WILL COME. That, in its essentials, seems to be the message. How seriously must it be regarded? Are other formulations more accurate representations of the truth?

The apparent exponential growth of population is one of the most familiar illustrations of how the warning can be inappropriate. Dr Meadows and his colleagues, more sophisticated than Malthus, declare at the outset that exponential growth is always the product of a positive feed-back loop. And it is true that the greater the number of children born, the greater will be the number of potentially fecund adults a generation ahead. In this sense, of course, in any population in which the net reproduction rate (the number of girl children per woman per lifetime) is greater than 1.00, exponential growth will take place with a time-constant determined partly by the breeding excess and partly by the interval of time between generations. So much is self-evident.

So how does it come about that Malthus's predictions of disaster for the British population (which took the best part of a century to respond with a lower birth rate to his pleas for moral restraint) failed to come to pass? Dr Meadows and his colleagues would have had a more convincing tale to tell if they had been seen to be more aware of where their predecessors went astray. And the truth is, of course, that the British population, like the population of the rest of Western Europe and North America, has in the past century and a half (but only just) gone through a period of historic change in which a reduction of death rate, often but not always the mainspring of population increase, has been followed by a reduction of birth rate and by a demographic condition which, taking one decade with another, can only be called stability. In other words, the demographic history of the now prosperous societies of the world shows plainly enough that in the end it is not famine and pestilence but a kind of restraint (which would nevertheless have offended Malthus by its dependence on techniques of contraception) which resolves the dilemma of exponential growth.

In circumstances like these, it is of course pointless to set about calculations of how many people will be alive in the decades ahead, and to base calculations of the annual consumption of resources on these estimates. The interesting questions are, instead, to know when the demographic transition will set in in the parts of the world where population is now growing quickly—and even to know whether there are some parts of the world



in which there is reason to fear that the demographic transition will not happen. Dr Meadows and his colleagues do, as it happens, point to the historical connexion between prosperity and birth rate—richer communities have lower birth rates. There is also a graph which shows how uniform appears to be the correlation between birth rate and GNP per head. But for a study which is supposed to be an assessment of the prospects for the decades immediately ahead, it is odd that Dr Meadows and his colleagues fail to point out that there is now good evidence that the countries of south-east Asia and the Caribbean are now well launched on a demographic transition which appears to be essentially similar to but if anything more rapid than the social transformations which brought demographic stability to Europe half a century ago.

The truth, which those who manipulate exponential growth curves seem consistently to overlook, is that there is nothing in the history of the past century to suggest that developing countries are intrinsically less capable than were developed countries of striking a sensible demographic balance, that many developing communities seem to be within a generation of such a happy state but that it is in everybody's interest that the laggards should quickly follow suit. In short, the problem of world population is not a simple problem in the exponential calculus but a complicated aspect of the evolution of society. And there is practical experience to show that in the encouragement of lower birth rates in the developing world, utterances from the Club of Rome may be less effective than humane steps to reduce the prevalence of infant mortality. Like a good many other attempts to predict the future condition of society, the Club of Rome and its calculators had forgotten the complexity, the diversity and the richness of society as it is.

The same weakness attends the calculation of the effects of economic growth on the future condition of society—the other chief plank in Dr Meadows's platform. In its essentials, the calculations of Dr Meadows and his colleagues echo the conclusions which are the central part of Dr Barry Commoner's argument in *The Closing Circle*. For does not economic growth imply exponential growth of the GNP, is there not a correlation between GNP and the consumption of resources such as metal ores and is there not also a correlation between economic activity (which usually implies industrial activity) and the pollution of the environment? These are the starting points for several of the calculations which the Club of Rome has now endorsed. Here again, unhappily, the subtleties are overlooked. Like other calculations of this kind, for example, the Club of Rome's document does not set out to describe the negative feedback loop which can be constructed by making the reasonable (and demonstrable) assumption that more prosperous communities are more eager than less prosperous communities to devote resources to the purchase of amenity, which may often consist of cleaner air or water or freedom from some other kind of pollution. And although the calculations of Dr Meadows and his colleagues do take into account the way in which the scarcity of natural resources of various kinds will be reflected in increased costs of these materials, they do studiously refrain from using the assumption that national resources are frequently positively correlated with increasing prices. In the circumstances, it may not be surprising that

their forward projections of the present so often seem to lead to conditions of instability or "collapse", as the saying goes. What this implies is that, for all their modest protestations to the contrary, Dr Meadows and his colleagues are trying to read too much into their necessarily rudimentary model.

The global aspect of these arguments is especially misleading. Dr Meadows and the executive committee of the Club of Rome make it plain that they base their claim on public attention on the world-wide character of their study. Although there is an acknowledgment in the committee's endorsement that there has been polite disagreement about the validity of predictions of global catastrophe based on global calculations with a single set of parameters, neither the authors nor their sponsors give sufficient weight to the objections which have been raised in the past few years to the way in which Professor Forrester's model, in its original form and as it is now applied to the purposes of the Club of Rome, lumps the problems of all communities under the umbrella of a single set of parameters. In terms of the discipline of systems analysis, which is said to have informed the study, what this implies is that the number of degrees of freedom is drastically reduced, which should at the very least imply that the conclusions should be accompanied by a warning that predictions of instability are almost by definition likely to be over-gloomy estimates. But the study, in common with others of its kind, also makes the quite distinct over-simplifying assumption that the historical path of industrial and social development which has been followed in the past two centuries by the United States will in due course be the path which other developing nations follow. The assumption that the development of an admittedly exceptional community will be the paradigm for all—or, as many would say, the assumption that one community can never learn from the mistakes of others—does at least deserve to be acknowledged as such.

It goes without saying that this catalogue of weaknesses in the first report of the Club of Rome should not be taken as an assertion that the growth and evolution of society occasion no problems. On the contrary, the social problems of poverty, disease and injustice are as pressing as they have ever been. (To its credit, the Club of Rome makes a point of urging that in the stable society to which it looks forward, it will be necessary to arrange that inequalities between rich and poor nations are somehow ironed out.) The overriding question, raised by the latest study as by several of its less expert predecessors, is whether the present circumstances are so dangerous that steps must quickly be taken to bring about a radical revision of the way in which society is organized. This, of course, is the spirit in which people such as Dr Paul Ehrlich, who considers that population growth is the immediate threat, gravely weigh the advantages and disadvantages of social innovations such as compulsory sterilization. Not so long ago (see *Nature*, **235**, 63; 1972) a group of British scientists lent their names to a document which urged a return to agriculture as the "backbone" of society, the organization of small communities and the restriction of personal mobility, geographical and presumably social. Other more moderate prophets argue for a more prudent regard for the common ground between communal and personal interests and, by doing so, echo the old vague but self-congratulatory sentiments of the Puritans. Although the formal study by Dr

Meadows and his colleagues leans in this direction, the Club of Rome itself has only generalities to offer. It asks for "radical reform of institutions and political processes at all levels" without saying what kind of reforms it has in mind. It asks for international planning on an unprecedented scale without saying what arrangements there should be for making plans and agreeing on them. And it asks for what the old evangelists would have called a change of heart without itself displaying a sufficiently sensitive understanding of the way in which society functions to compel the allegiance of those outside the Club of Rome. Mr Peccei and his colleagues in the club should try to do better next time, and they should recognize that in present circumstances, as in the past, the prophecies most likely to be listened to are those which are accompanied by constructive suggestions about what to do. This, unhappily for them, requires more than mere computation.

Which Ducks are Lame?

ON the face of things at least, the British Government appears to be in rapid retreat from its declared policy that industry must learn to stand on its own feet. Mr John Davies, Secretary of State at the Department of Trade and Industry, let it be known soon after he came to office that industrial lame ducks could expect no help from him. His supporters are understandably chagrined that last week he agreed to provide £35 million as a subvention for the company which has been set up to try and make a success of the shipyards on the upper Clyde and that this week he has agreed to provide £100 million by way of subsidy for the National Coal Board as well as increasing its borrowing powers from the Treasury by another £50 million. The fact that the price of coal will also be increased by $7\frac{1}{2}$ per cent is, of course, a simple consequence of the Wilberforce pay award (see *Nature*, 235, 409; 1972). On the face of things, all this appears to be a great defeat for the government's policies even if one of the pressures with which the Department of Trade and Industry has to contend is the fear that a further increase in unemployment would be politically intolerable. In one sense, at least, the new subventions for British industry are ways of providing jobs for men who would not otherwise be economically employed. The truth, of course, is that in the short run there may be virtue in such a course of action, inflationary though it may be. But a much more serious weakness in the government's policy is that it is doing very little to ensure that the jobs now being squeezed out of the British economy by competition from abroad are replaced by other ways of earning a living. On the long view, the most urgent need is for a constructive policy on industrial research and development.

What are the directions in which new opportunities should be sought? Where will jobs be found for all those who will be made redundant from the British coal mines in the years ahead, perhaps 50,000 people altogether? What will happen to those displaced from the shipyards when the subsidies have been expended? And what, in any case, is to be done to employ the million or so who are at present unemployed? Plainly, there is no sense in considering these questions in isolation from the

prospects of Britain's entry to the European Community less than a year from now. It is not too soon to ask whether civil engineering is properly organized to be competitive on a European basis. Although West Germany has what would seem to be a commanding advantage in heavy mechanical engineering, there is also much that could be done to strengthen the British companies which are traditionally strong in the manufacture of machine tools, for example. But there are plainly great opportunities in nuclear power if only the British industry can be cast into a competitive pattern and if, by intelligent research and decisive development, it can be given tangible goals at which to aim. And then, of course, there is the whole field of telecommunications where Japanese companies in the past few years have demonstrated quite clearly that both market and job opportunities exist. In short, there is no lack of fields in which new prosperity might be found. The problem which only the government can solve is to make them accessible.

Ironically, the sums of money now being spent to help Mr Davies's lame ducks are very much larger than those needed to give the industries concerned a proper sense of enterprise. The most obvious gap in the government's present arrangements for sponsoring development in forward looking industries is that there is no machinery for channelling funds for research and development into potentially profitable paths. So does it not follow that the most constructive escape from the government's present dilemma in its economic policy is the setting up of larger and more effective organizations for supporting industrial research?

100 Years Ago



DR. LIEBREICH, the eminent ophthalmist, of St. Thomas's Hospital, delivered a lecture at the Royal Institution on Friday evening last, on certain faults of vision, with special reference to Turner and Mulready. The later "aberrations" of Turner's style he attributed to a physical change in the refractive power of the eye, by which illuminated points were converted into illuminated lines. The change of manner in Mulready's later pictures he accounted for, in like manner, by increasing yellow degeneration of the crystalline lens. We hope in a future number to give a report of the lecture.

WE are very glad to be able to state that intelligence has just been received from Prof. Huxley that his health has already been greatly renovated by the pure air of Upper Egypt. He wrote from Thebes, and was then contemplating a visit to Assouan, from which he would probably have returned to Thebes before this.

WE understand that the Meteorological Committee have resolved to issue lithographed illustrative charts of the Daily Weather Report, which will be delivered in London, within a reasonable distance from the office of the printer in Lincoln's Inn Fields, between 1 and 2 P.M., or posted in time for the evening mails. Up to the 31st of March these charts will be supplied gratuitously.

From *Nature*, 5, 390 and 391, March 14, 1872.

OLD WORLD

Criticisms of Rothschild Reiterated

LORD ROTHSCHILD's proposals for restructuring the funding of the Natural Environment Research Council were described last week by its chairman, Professor F. H. Stewart, as "arbitrary and based on a misconception of what NERC does". Professor Stewart was one of six witnesses—the others being the secretary of the council and four directors of NERC establishments—appearing before the Select Committee on Science and Technology, which is to produce a report on the controversial green paper before Easter.

Professor Stewart said that NERC has no quarrel with the customer-contractor principle as such, but that the way in which Lord Rothschild had chosen to apply it in table 4 of his report revealed a very large discrepancy between his thinking and the views of the council. According to Professor Stewart, only about £1 million of NERC's annual budget of £15.3 million can be described as research done for one dominant customer, so only this amount could reasonably be turned over to government departments and spent strictly according to the customer-contractor principle. Between 70 and 80 per cent of NERC's research can quite properly be dubbed strategic, Professor Stewart said, and, in terms of customers and contractors, much of the applied research and many of the advisory services are satisfying the needs of many customers. He cited the advisory service run by the Institute of Geological Sciences which is used by six government departments, local authorities, water boards, industry and universities.

If Lord Rothschild's plans are implemented in full, NERC would only receive £7.7 million from the Department of Education and Science, and the council says that after allowing for expenditure on the British Antarctic Survey, the research vessel base, the Geological Museum and support in universities, "only a derisory sum would be left for major capital programmes and the fundamental work in NERC institutes".

Professor Stewart said that on neither of the two occasions on which NERC members met Lord Rothschild before he drafted his report were any more than the generalities of the customer-contractor principle discussed, and that an invitation to Lord Rothschild to discuss the specific research programmes financed by NERC was never taken up.

Professor Stewart did not feel that better accountability would go hand in hand with implementation of the Rothschild proposals, because at the moment expenditure of more than £50,000 has to be sanctioned by the Department of Education and Science, and NERC is anyway overlooked by the Council for Scientific Policy. And, after critical scrutiny of their programmes, the CSP makes recommendations each year about the way in which the money available to the research councils should be distributed.

Professor Stewart said that rumours of impending change had dogged NERC since it was set up in 1965, and that, for example, talk of moving the Institute of Geological Sciences to a government department implied criticisms that were never formally voiced and could, therefore, not be replied to.

Dr M. E. D. Poore, director of the Nature Conservancy, said that his staff are worried about the future, and had been throughout the 1960s—especially when the suggestion of dividing the conservancy into a research arm and a conservation arm was being actively canvassed. Dr McCulloch, director of the Institute of Hydrology (which Lord Rothschild would have as part of the Department of the Environment), said that his staff are "seriously concerned" at the prospect of a loss of identity. None of the witnesses felt, however, that work is suffering as a result of the present uncertainties.

Dr Poore said of the Nature Conservancy that its executive function as a conservation body "has suffered" as a result of inclusion in NERC, because funds for this function have to be judged by the same criteria as the rest of NERC's research. Professor Stewart said that on balance the council felt it better that the Nature Conservancy should remain as an integral body under NERC's auspices.

At a later session the select committee canvassed the views of the Institution of Professional Civil Servants (IPCS) and the Association of Scientific, Technical and Managerial Staffs. The IPCS said that it "strongly supported Rothschild's idea of strengthening the scientific capability of departments". It is important to have a chief scientist capable of permeating the department with scientific ideas and to do this the IPCS proposes the establishment of customer boards within government departments.

But despite its approval of some of

Lord Rothschild's proposals, the institution is still critical of certain aspects of the green paper. "There is a strong implication," it states in its memorandum to the select committee, "doubtless unintentional . . . that hitherto government departments have been frittering away the nation's resources by undertaking a large variety of projects devised by and of interest only to scientists without departmental control. The implication is unjustified and resented." Further, Mr W. McCall, general secretary of the institution, said that it is important, despite Rothschild's assertion that the Haldane principle is outdated, not to reject that principle completely. "That," said Mr McCall, "is why we are deeply attached to the research council system"; he emphasized, however, that government departments should nevertheless be able to carry out the research they feel is required.

The IPCS also made it clear that it supports the need for proper accountability, and feels that with members from research establishments, industry and the departments its proposed customer boards would help to improve policy making within departments. The institution also questions the wisdom of Rothschild's proposal of a chief scientist and a controller of research and development. Such an arrangement may be satisfactory within the Ministry of Defence, said Mr McCall, but in other departments it might be better to have one man at the top with real power, and two organizations—one dealing with the customer aspect and one for research and development—below him.

Mr McCall also said that the institution is strongly in favour of the proposed 10 per cent surcharge on applied research, although he felt the figure to be a purely arbitrary one, which ought perhaps to vary between ten and fifteen per cent according to the nature of the work.

In conclusion the institution said that if, as a result of the implementation of the Rothschild proposals, expenditure by the research councils does fall by 10 per cent a year—the maximum envisaged by Lord Rothschild—then the results would be "devastating" from the point of view of the institution as a trade union.

The Association of Scientific, Technical and Managerial Staffs (ASTMS) confined its evidence chiefly to the Medical Research Council, which employs more ASTMS members than any

other council. The association was at pains to point out in its opening remarks that it does not take sides in the debate between Rothschild and Dainton—a neutrality for which Mr Ronald Brown later took it to task. The association seriously questioned the value of the figures in tables 2, 3 and 4 of Lord Rothschild's report, suggesting that they "were ridiculously arrived at".

The ASTMS said that it accepts the customer-contractor principle if applied to tactical research because it has seen it at work within industry, but the association emphasized that it does not trust the customer to ask the right questions when it comes to strategic research—particularly when that customer is the Department of Health and Social Security, which "is not properly briefed in such matters".

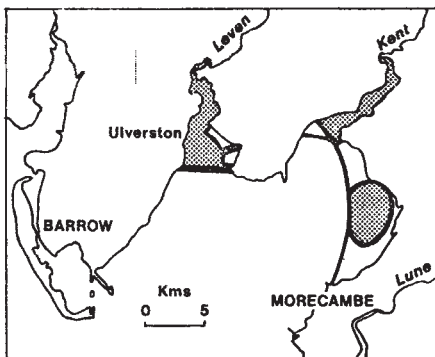
When questioned about the size of the supporting staff for a chief scientist, the association said it thought the staff should be large and not completely full-time. The MRC, said the association, has a large number of expert committees, but, even so, it is difficult to assemble sufficient expertise. A large number of part-time members would help to do this, and would ensure that scientists did not get out of touch working solely in a government department.

The ASTMS concluded—as did the Institution of Professional Civil Servants—that the consequences would be "disastrous" if Rothschild's proposals were implemented in full unless it was clearly seen that the relationship between the research councils and the departments was one of cooperation. The association also claimed, in its written evidence, that the timetable for introducing the changes is "totally unacceptable"; no far reaching changes should be undertaken in less than one year. "The Rothschild report," the memorandum says, "bears all the hallmarks of a hurriedly prepared document . . . to make fundamental changes in government research in Britain on such a basis would be reckless."

WATER RESOURCES

Four Scheme Mix

THE publication of the full engineering study of the Morecambe Bay scheme last week has presented Britain's planners with a multiplicity of choices. Of the various schemes studied (see *Nature*, 235, 423; 1972), the Water Resources Board states that if water conservation were the only consideration, then scheme III would be the right choice. This involves the construction of barriers at the rivers Kent and Leven, the construction of a reservoir below Silverdale and one off Cark. But, although the provision of 2,050,000



The Water Resources Board's new hybrid scheme.

m³/d is the central consideration of the scheme, it is factors other than water conservation that will eventually decide which scheme is chosen.

The board advises against any of the three schemes which allow roads to be built over the top of the barrages to Barrow, principally on the grounds that they could cause heavy siltation near Heysham, but in the long term it may be decided that the possible benefits of the road will outweigh the disadvantages. If a road is needed, then the board recommends scheme IIb, which, in spite of the possibilities of siltation at Heysham, is the scheme which the Nature Conservancy favours most, although it would rather not see any form of water storage in the bay, and is particularly opposed to any reservoir off Cark.

An alternative that the board suggests is to build a hybrid scheme in stages, starting with a Leven barrage and adding the Kent river barrier later.

The complexity of the situation is underlined by the separate report of the Economic Study Group on the scheme, which is twice as large as the board's engineering report. In the coming months, not only will the pros and cons of the various schemes have to be set against each other, but also the whole question of whether the future of Britain's water conservation lies in estuary schemes rather than inland reservoirs will have to be decided. The Water Resources Board's report on the future pattern of water storage and supply for England and Wales is to be published later this year or early next, when the board will decide its views on whether or not the Morecambe Bay scheme should be built.

GENETICS

Vavilov Commemorated

THE genial face preserved in stone on the wall of the Institute of Genetics of the Academy of Sciences in Moscow is an outward sign of the reinstatement of the reputation of Professor Nikolai

Ivanovich Vavilov. In 1940, after six years working at the institute, he was ousted by the notorious anti-Mendelian T. D. Lysenko, and three years later he died in Siberia. He is thought to have spent some time before his death in prison while Lysenko's views held sway.

Vavilov, who was born in 1887, studied at the University of Cambridge under Professor W. Bateson and also at the John Innes Horticultural Institute then based in London, after graduating from the Agricultural Academy at Petrovsko-Razumovskoe near Moscow. From 1917 to 1921 he was professor of botany at the University of Saratov, from where he went to what eventually became the Lenin All-Union Academy of Agricultural Sciences.



He built up a strong international reputation as a plant geneticist, being particularly noted for his work on the origin of cultivated plants. By making expeditions to Persia, Afghanistan, Abyssinia, China and other regions he collected plant material on which he based his hypothesis that countries with the greatest number of varieties of a particular plant are the areas of origin of that plant. When in 1942 he was elected a foreign member of the Royal Society, *Nature* commented that he had become the leading taxonomist of cultivated plants as well as doing valuable plant breeding work.

Vavilov's contributions are now publicly acknowledged by the plaque, which was unveiled on November 26 last year on the eighty-fourth anniversary of his birth. The inscription reads: "In this building from 1934 to 1940 worked the eminent biologist, Academician Nikolai Ivanovich Vavilov".

NEW WORLD

A Stringent Recipe for Viability

by our Washington Correspondent

In these times of financial stringency, in which relevance is the key to securing funds for scientific projects, a subject as esoteric as high energy physics has been going through a tough time in the United States. Declining funds have pushed the national programme "to the edge of being viable", Dr Paul W. McDaniel, director of the AEC's division of physical research, told the Joint Committee on Atomic Energy last week. And those sentiments were echoed by a string of witnesses who came to Washington for two days of hearings on the AEC's high energy physics programme—the committee's first detailed look at the subject since 1965.

Nevertheless, there are signs that funding may have reached its nadir, and although there will undoubtedly still be some belt tightening to do in a few laboratories, prospects look brighter now than at any time in the past few years. For one thing, after a period of absolute decline in funds—even before inflation is taken into account—the Atomic Energy Commission is asking for a modest increase in the operating budget for the six remaining national accelerators. Moreover, almost on cue for the committee's hearings last week, the proton accelerator at the National Accelerator Laboratory at Batavia, Illinois, reached its design energy of 200 BeV for the first time, on schedule and within budget.

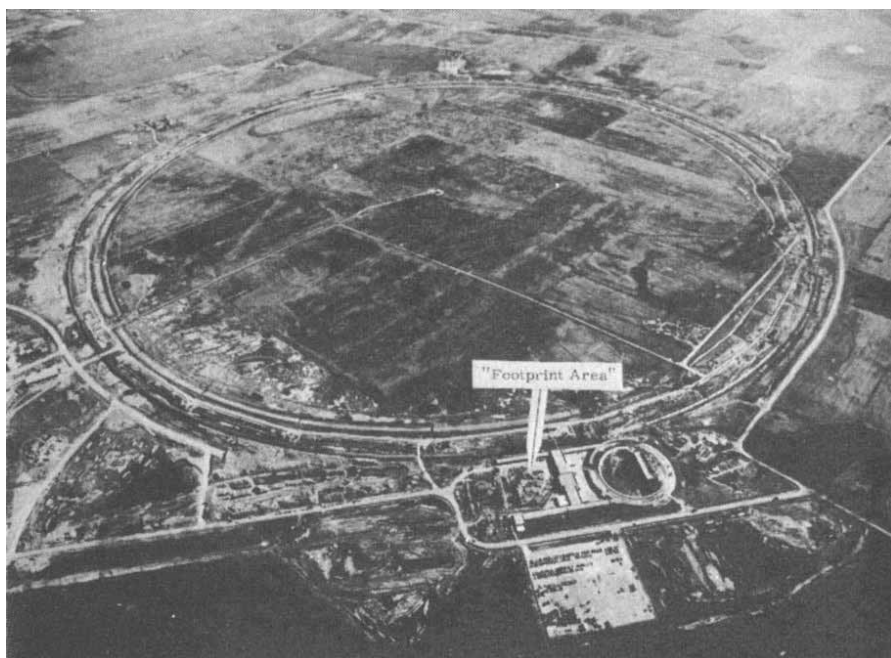
The epitome of "big science", high energy physics is conditioned by the fact that new facilities require massive capital outlays for building, and relatively large annual injections of funds to operate. Moreover, unlike cancer researchers, for example, high energy physicists are unable to justify requests for funding increases on even vague promises of practical benefits and must instead rely on the more intangible and therefore less politically appealing argument that high energy physics is probing deep into fundamental questions concerning the constituents of matter.

The result is that, since 1968, operating funds for the Atomic Energy Commission's high energy physics programme (which accounts for about 90 per cent of the total national programme) have declined. But, superimposed on the declining budget, the 200 BeV accelerator at the National Accelerator Laboratory (NAL) has been taking a growing share of the funds

and the relatively new Stanford Linear Accelerator (SLAC) has also cornered a larger chunk of the total operating budget. The upshot is that the whole programme has been severely squeezed, with the following consequences:

- Since 1967, manpower supported by the high energy physics programme, excluding the National Accelerator Laboratory, has dropped by about 30 per cent, and since 1969, even with the growth of NAL taken into account, manpower reductions have amounted to more than 20 per cent.
- The Atomic Energy Commission has

the Princeton-Pennsylvania accelerator, a machine which cost \$40 million to build and which still had plenty of research left in it, as much as anything stimulated the Joint Committee's concern over the viability of the high energy physics programme, for in its report on the AEC authorizations last year, the committee pointed out that operating budgets for the remaining accelerators must be sharply reversed if the United States is to remain in the forefront of high energy physics research. The committee therefore asked the Atomic Energy Commission to take a close look at its programme



The National Accelerator Laboratory: 200 BeV on cue.

withdrawn support from three accelerators — the Princeton-Pennsylvania Accelerator, the CalTech Synchrotron and the Brookhaven Cosmotron—and converted the Cambridge Electron Accelerator from a multi-purpose machine to a single-purpose colliding beam device, with a consequent drop in support.

- Use of the remaining accelerators has declined to some 60 per cent of their practical capacity, but to maintain operations even at this reduced level, research and development on new accelerators and new accelerator devices has been sharply cut back.

Withdrawal of the AEC's support for

and to recommend a minimum level of support necessary to keep each of its accelerators viable and productive, and to develop a priority list of which facilities should be shut down if future funding decreases below the minimum suggested.

The report, delivered to the Joint Committee at the opening of the hearings last week, is clearly not a planning commitment, since it was produced in response to the specific request for an evaluation of minimum acceptable funding levels, but it nevertheless provides some important clues to the likely developments in the US high energy physics programme.

One thing that the report makes clear,

for example, is that the commission will fight hard to prevent any more accelerator shutdowns. The AEC points out that each remaining device is unique with respect to its beam characteristic, ancillary facilities, secondary beams and so on, so that to provide a priority listing is "somewhat like the task of determining which has greater priority, the right leg or the left arm". Nevertheless, for what it is worth, the commission suggests that it would give highest priority to the 200 BeV accelerator; second on the list comes the Alternating Gradient Synchrotron at Brookhaven and the Stanford Linear Accelerator; on the third rung are the Zero Gradient Synchrotron at the Argonne National Laboratory and the Bevatron at the Lawrence Berkeley Laboratory, and lowest on the listing comes the Cambridge Electron Accelerator.

But even if funding were to fall below the level at which the commission believes each facility would be viable and productive, the report suggests that the best course of action is not necessarily to eliminate the lowest priority facility. A better solution, the AEC suggests, "might even be to increase its support somewhat and decrease the support of a higher priority facility, in the interests of better programme balance and perhaps better overall programme viability and productivity". Another suggestion mooted by the AEC is that the programme scope of some facilities might be reduced if funding were to decrease even further, as, for example, the Cambridge Electron Accelerator has been revamped.

While the remaining laboratories can be fairly confident that their funds will not be cut off entirely, however, they can also be sure that they are not about to experience a bonanza. The AEC report makes clear that the operating budget for the National Accelerator Laboratory will grow over the next five years, while budgets for the base programme—the remaining five accelerators and the university research programme—will remain at about the level projected for 1973. In other words, recent trends which have seen the 200 BeV machine soaking up a growing share of the total budget are likely to be repeated and perhaps even intensified (see Table 1).

Another implication of the funding pattern suggested in the report is that the National Accelerator Laboratory will be run in 1977 at about 70 per cent of its full capacity, which is somewhat higher than the other accelerators, but still considerably less than was being talked about a year ago. The slower growth rate in the operation of the 200 BeV machine, together with a holding operation on the other accelerators, would mean that the university research programme would also grow rather

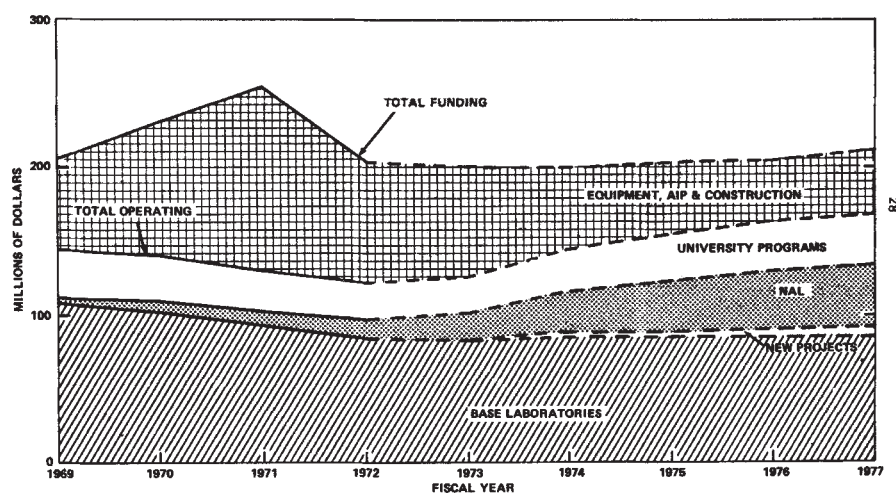
slowly in the period 1974 to 1977.

An important aspect of the AEC's suggested programme for high energy physics is that it would arrest the erosion of manpower that has been taking place during the past few years, and if the national laboratories were assured of such a stable base programme, they would be better able to plan their manpower levels. One particularly striking result of the financial cutbacks over the past few years has been a sharp drop in the number of graduate students supported by the AEC high energy physics programme. In 1968, for example, more than 800 students were taking part in AEC sponsored research, but in 1972 the numbers had declined to just over 500. Whether the reduced programme and the steadily declining numbers of physicists supported by it still provide a sufficient incentive to

considered are a beam recirculator for the Stanford Linear Accelerator, which would double the energy of the electron beam. This would be in addition to the electron-positron storage rings, a device in which electrons and positrons are circulated in opposite directions and made to collide at very high energies, which should start operating this summer.

A ring of superconducting magnets placed above the main ring of the 200 BeV is also being considered by the AEC, although planning at present is at a very early stage. This device, which would probably cost between \$10 and \$20 million, would double the energy of the proton beam, giving the machine a possible energy of 1,000 BeV. (Dr Robert Wilson, director of the National Accelerator Laboratory, said last week that the present machine

Table 1 AEC High Energy Physics Programme—Annual Costs (FY 1973, Dollars)



attract good talent and then to keep it is clearly one of the aspects which greatly concerns the AEC, for it is this factor on which will depend the US capacity to remain in the forefront of high energy physics.

The report also suggests that at least \$3 million should be set aside each year for accelerator improvement projects, the importance of which "cannot be overemphasized". Pointing out that accelerator research and development has been sacrificed to an unhealthy extent during the budget cuts of the past few years, the AEC report says that these reductions "are strong indications that future viability is in danger". Nevertheless, there is a host of projects in line for upgrading the capability of existing machines, and some of these improvements will be financed in the 1974 financial year.

Among the candidates being con-

sidered should be able to reach about 500 BeV, the only limitation at present being the adequacy of the power supplies to take such a demand of electricity without a storage device.)

Other possible upgradings include a 25 foot diameter bubble chamber for the National Accelerator Laboratory and high energy intersecting storage rings. One proposal for the Brookhaven National Laboratory is for a device which would inject protons into a storage ring at about 30 BeV, from the alternating gradient synchrotron, and then slowly accelerate them over the course of several minutes with superconducting magnets to an energy of about 200 BeV.

With the AEC's determination to maintain the base programme at least at its present level and to allow improvements to be made to existing accelerators in the next few years, high energy

physicists can rest a little easier than they have in recent years, and one remark made during the hearings has at least not gone unnoticed in the physics community. When Dr McDaniel detailed the AEC request for funds for physical research in 1973, Melvin Price, the committee chairman, remarked, "We may even do better than that."

TECHNOLOGY ASSESSMENT

Down the Home Straight

by our Washington Correspondent

THE proposal to establish an Office of Technology Assessment in the legislative branch of the Federal Government seems now to be assured of success. To judge by the tone of hearings on the proposal, held last week by the Senate Rules Committee, the concept is agreed upon by key members of Congress from both political parties, and the chief remaining doubts about the proposed office concern the membership and powers of its management board.

A bill to establish the office was passed early last month by the House of Representatives, but an amendment which caught its sponsors by surprise changed the constitution of the board so that instead of consisting of eleven members, only four of whom would be Congressmen, the office would be directed by a board consisting of five Senators and five members of the House of Representatives. Proposed by Mr Jack Brooks of Texas, the amendment would effectively mean that the office would be controlled by a joint committee of Congress in place of a rather more independent board of directors.

During the three weeks that elapsed between the bill's passage by the House of Representatives and the hearings before the Senate Rules Committee, Mr Brooks's amendment picked up at least two important supporters in the shape of Senator Gordon Allott and Senator Edward M. Kennedy, both of whom sponsored the original legislation in the Senate. Kennedy testified last week that he agrees with the intent to limit the membership of the governing board only to Congressmen, but suggests that ten should be drawn from each house.

Supporters of the original proposal are, however, concerned that an arrangement in which the Office of Technology Assessment is governed by a joint congressional committee would be less responsive to public demands. As John Davis, chief sponsor of the legislation in the House of Representatives, suggested, for example, Congressmen have little time to devote to extra committee duties, and the proposal could therefore result in less efficient direction.

It seems likely, however, that a compromise will be struck between the original proposals and those contained in Mr Brooks's amendment. Both Mr Davis and Mr Kennedy suggested last week that if the board does consist solely of Congressmen, it should be augmented by an advisory committee drawn from members of the public and perhaps including the Comptroller General and the Director of the Congressional Research Services. The suggestion is that the advisory committee would consist of members of the public drawn from a variety of backgrounds which would be useful in

assisting the board of directors in formulating policy for the office.

Testifying in favour of the proposal last week, Dr Philip Handler, president of the National Academy of Sciences, said that he hopes that the office will not regard itself as a policeman whose chief mission is to put a brake on science and technology. He pointed out that technology assessment has in the past been carried out chiefly by an agency that either wants to forward a technology or by a group that wants to prevent it, but rarely has there been a balanced attempt to look at both the benefits and disadvantages of projects.

Short Notes

Higher Education

THE chief provisions of the higher education bill that was passed last week by the Senate were almost completely obscured by the acrimonious debate over school busing amendments that were tacked on to the bill. Nevertheless, the Senate reaffirmed its belief that college students should be given federal support grants, the amount being based on parental income, and that colleges should receive general institutional grants tied to the number of federally-aided students that they have enrolled. The student grant provision is expected to increase the number of federally-aided students by a factor of six.

The only major amendment that was made to the bill, compared with the measure that was passed by the Senate last year, was a proposal by Senator Birch Bayh which would prohibit discrimination in colleges and universities on the basis of sex. Bayh's amendment would cut off federal aid from colleges which violate a ban on sex discrimination in their admissions policies and in their staff policies, but it would not apply to those colleges that have traditionally admitted members of only one sex. The bill passed by the House of Representatives, on the other hand, does not include admissions policies in its ban on sex discrimination. Both the House and the Senate bills are now ready to go to a conference committee where fundamental differences in their approach to institutional and student support must be reconciled.

Nuclear Testing

A MODERATE groundswell of opinion seems to be building up in the Senate in favour of a ban on underground nuclear testing. In January, Senator Edward M. Kennedy introduced a Senate resolution urging the United States to declare a moratorium on underground nuclear testing for as long as the USSR refrains from such tests,

and he also called for an immediate start to be made on negotiations for a formal treaty. Similarly, a bipartisan resolution was introduced into the Senate last week by Senator Philip A. Hart and Senator Charles Mathias, urging that negotiations be instigated immediately for a complete ban on nuclear testing. The Hart-Mathias resolution has gained an impressive list of supporters from the scientific community, including Harrison Brown, foreign secretary of the National Academy of Sciences, Franklin Long of Cornell University, Herbert York of the University of California at San Diego, George Wald of Harvard, George Kistiakowsky of Harvard, Polykarp Kusch of Columbia University and Bernard Feld of the Massachusetts Institute of Technology.

Marine Science

A REPORT published last week by the National Research Council suggests that all the programmes of the United Nations dealing with marine science should be combined in a single and separate organization. Prepared by a panel of the NRC's committee on oceanography, under the chairmanship of Dr William T. Burke of the University of Washington, the report points out that international cooperation on marine science is becoming more important in the light of increases in the variety and intensity of ocean uses, but it questions the ability of present international arrangements to meet the task. Specifically, the panel recommends that a new UN organization should be set up to provide technical support to other international organisations concerned with management of ocean resources and with the political aspects of ocean affairs, and that in the United States the National Oceanic and Atmospheric Administration should be the chief government agency responsible for coordinating international exchange of data on ocean affairs.

NEWS AND VIEWS

Archaeology using Mathematics

ONLY twenty years ago the notion that mathematics could play a significant part in archaeological or historical thinking seemed paradoxical. The book of nature might be written in the language of mathematics, as Galileo remarked, but history and prehistory concern themselves not with solid bodies or molecules but with human beings, and a quantitative approach was not considered appropriate or indeed proper. The newly published proceedings of the Anglo-Romanian conference, *Mathematics in the Archaeological and Historical Sciences* (edited by F. R. Hodson, D. G. Kendall and P. Tăutu, Edinburgh University Press, 1971) demonstrate very effectively how far archaeology has travelled since those days.

With the publication in 1951 (W. S. Robinson and G. W. Brainerd, *American Antiquity*, 16, 293) of a numerical method for setting assemblages of archaeological objects in chronological order ("seriation") a serious effort was made to formulate explicit procedures for some of the tasks in archaeology formerly intuitively undertaken. More recently, and under the influence of developments in related disciplines summarized in works such as Peter Haggett's *Locational Analysis in Human Geography* (Arnold, London, 1965) and *Numerical Taxonomy* by Robert R. Sokal and Peter H. A. Sneath (W. H. Freeman, San Francisco, 1963), a wide variety of quantitative techniques has been applied in archaeology, with some measure of success.

The results, as well as providing a series of new insights into the past, have certainly proved controversial. On the one hand zealots have emerged who foresee the transformation of the whole subject of prehistory into an ordered hierarchy of law-like statements, many of them formulated in quantitative terms. They look towards the day when "archaeological general theory" will command the same wide respect as the logical organization of more developed sciences such as physics.

At the other extreme stand the recalcitrant innumerate, proclaiming themselves the last defenders of humanism. Some of the fears of this committedly "humanist" school of thought have been very cogently expressed in an article by Jacquetta Hawkes, "The Proper Study of Mankind" (*Antiquity*, 42, 255; 1968), where, speaking of mathematics and the sciences in general, she sees a difficulty "in preventing the scientific and technological servant from usurping the throne of history".

The 1970 conference illustrates well how both these extremes are misguided. The occasion was the first time that such collected mathematical expertise has been brought to bear upon archaeological problems (with the possible exception of the conference papers published by the Centre National de Recherche Scientifique in 1970 under the title *Archéologie et Calculateurs*). The maturity in approach is best seen in the relatively restricted nature of the problems tackled. There is no tendency to grandiloquence, no attempt to set up widely or universally valid models for human behaviour in the prehistoric past. Nobody need feel that the throne of

history has been usurped, nor that archaeology has been transformed overnight into one of the natural sciences.

Instead specific technical problems were considered, notably in the fields of taxonomy, multidimensional scaling, seriation and the study of evolutionary tree structures among written documents, languages and human evolution. As one contributor aptly remarked, "there exists no mathematical history and no mathematical archaeology but only history using mathematics and archaeology using mathematics". Naturally some of the approaches are novel—for example, the contribution using decision theory to construct "A Model of Michael the Brave's Decision in 1595"—and others, such as "A New Approach to a Problem of Chronological Seriation associated with the Works of Plato", seem at first sight (and without good reason) slightly incongruous for their use of numerical methods in what may be unexpected fields.

Probably of greater significance than these departures, however, is the success which numerical methods are now having in the classification and ordering of archaeological materials. Indeed it seems that many of the outstanding early problems in the sorting of artefacts into meaningful clusters, or in ordering them into chronological series, have now been solved. This is of fundamental importance to the palaeolithic period especially, where so much of the available evidence is in the form of assemblages of chipped stone tools. These can readily be compared using a number of measurable and comparable variables, often in terms of the concepts of "similarity" and "distance", central to numerical taxonomy. Techniques have been developed which allow of far better and more efficient classifications than could ever have been produced by traditional methods.

Mathematics, then, is proving useful in solving a number of problems in archaeology, and their range is bound to increase. There is nothing astonishing or threatening in this, nor is the whole nature of archaeology being transformed. The rather artificial boundaries sometimes thought to delimit the proper fields of interest of the mathematician and the archaeologist are disappearing, and there is a good deal of common ground. Now that the dusts of controversy are beginning to settle, it is possible to see that mathematical techniques are taking their place beside those of physics and chemistry as valued and indispensable aids to the archaeologist.—From our Archaeology Correspondent.

Plasmas and Lasers

IN the past decade the scattering of a laser beam from density fluctuations in a plasma has become one of the most reliable and respected techniques in plasma diagnostics. In this type of measurement the free electrons are the scattering agents and, in principle and often in

practice, it is possible to derive the density, the velocity distribution of the electrons and ions, the degree of turbulence and the magnetic field from the spectral intensity of the scattered laser light. The Thomson cross-section for photon scattering from free electrons in the plasma, although small at $6 \times 10^{-25} \text{ cm}^2$, is always much higher than that for scattering from bare ions and is generally higher than Rayleigh scattering from atoms or molecules.

Recently Burrell and Kunze of the University of Maryland have highlighted a new and powerful scattering technique—the use of tunable dye lasers to effect “resonance scattering” from excited states of atoms or incompletely stripped ions in the plasma (*Phys. Rev. Lett.*, **28**, 1; 1972). The cross-section for resonance scattering can be many orders of magnitude higher than the classical Thomson cross-section for scattering from free electrons. It is possible therefore to detect scattering from such low concentrations of test atoms that the energy balance in the plasma is not affected. Dimock, Hinnov and Johnson (*Phys. Fluids*, **12**, 1730; 1969) have pointed out that with available dye lasers a detectable enhancement can be achieved by resonance scattering from Ba^+ ions seeded into a plasma with a concentration as low as $10^5 \text{ ions cm}^{-3}$.

The principle is to select the frequency of the photons from the dye laser photons to match the frequency of a transition in the test atoms or ions. The laser beam is absorbed in transferring electrons from the lower level of the transition to the upper levels where they are transiently captured. This distortion to the equilibrium population of the levels is termed “optical pumping” and has been widely used for population inversion in lasers, in magnetometry and for frequency standards where hyperfine Zeeman components are selectively pumped using microwave or radio-frequency beams.

On increasing the intensity of the dye laser pulse the population of the upper level will grow until there is equality with the population of the lower level. Above this laser intensity, which is not difficult to achieve in many practical situations with dye lasers, the emission is independent of the laser power. If the decay time of the upper levels is much less than the duration of the laser pulse, then the emitted intensity is also independent of the pulse duration. The overpopulation of the upper levels, relative to the unpumped condition, will decay by spontaneous emission (fluorescence) and will be redistributed by collisions among the other levels in the term scheme.

It is clear that by adjusting the length of the irradiating pulse and by observing the intensity of other transitions which are collisionally coupled to the pumped levels, it is possible to derive collisional rates between excited levels. When collisional decay can be ignored, as for low density plasmas, an overpopulation of long-lived or metastable upper levels can give information on the spread in time of the spatial distribution of the disturbed atoms. A second laser pulse is delivered to the plasma as a probe, at some distance from the pumped volume, to de-excite the test atoms and so derive the plasma drift (Dimock, Hinnov and Johnson, *ibid.*).

In the sense that there is a finite time interval before the disturbed level populations relax, the resonance technique is not true scattering. “Scattering” would be more appropriately applied to the conditions where the laser is

tuned off-resonance to some virtual level whence the re-emission time is negligibly short. This “off-resonance” or Rayleigh scattering scales as $\nu_0^4 (\nu_{ul}^2 - \nu_0^2)^{-2}$ (where ν_{ul} is the transition frequency between the levels u and l , and ν_0 is the frequency of the dye laser and can exceed the Thomson scattering cross-section. Rayleigh scattering has been observed, for example, in plasmas even when ν and ν_0 are 400 Å apart in the visible. The spectral intensity of the Rayleigh scattered light also reflects the local velocity distribution of the atoms, although in a complicated way.

Burrell and Kunze investigated a weakly ionized helium plasma in which the 4^3D levels of neutral helium were pumped from the $2p^3P$ levels with a ten nanosecond dye laser pulse tuned to 4471 Å. From the enhancement of the emission which was also observed from other levels collisionally coupled to the 4^3D levels, it was possible to derive the corresponding rate coefficients. From the decay time of the fluorescence after the end of the dye laser pulse radiative rates could also be deduced. No enhancement was observed when the dye laser was tuned “off-resonance”.

It is fair to say that the interpretation of the enhancement emission would be difficult without some prior knowledge of the collision rates among the excited levels, and this requires values for the temperature and density. These plasma parameters can most conveniently be measured by scattering from the free electrons so that the resonance scattering and Thomson scattering are complementary. Most important, both techniques are local measurements in the plasma and in both cases the spectral intensity of the scattered radiation yields the velocity distribution of the scattering particles.

The merits of resonance scattering are:

- Scattering is observed from low concentrations of atoms and ions, which may be present inevitably as charge-exchange neutrals or as test ions seeded into the plasma, in which case the technique is perhaps restricted to plasmas of relatively low temperature with a high population of excited states which give rise to visible transitions. On the other hand there may be some applications in laboratory astrophysics for optically pumping between the ground terms of those highly-ionized ions which give rise to the visible coronal lines, for example.
- The spectral intensity of the scattered light reflects directly the local distribution of irradiated ions which—if the test species is in equilibrium with the main body of plasma ions—gives the local ion temperature.
- Streaming motion and diffusion of the ions can be monitored using two separate irradiating laser pulses.
- On optical pumping Zeeman components with a polarized dye laser, the direction of the field can be measured in a magnetized plasma from the plane of polarization of the fluorescence.
- Collisional rate coefficients and radiative decay times of levels in the test ions can be measured using short duration pulses.

Dye lasers now exist which can cover almost all of the visible spectrum and, with some development, will inevitably encroach on the ultraviolet and near infrared. Because their frequencies can be tuned, and because of their flexible pulse duration, high intensity and variable bandwidth, they will clearly have many applications in diagnostics based on the scattering of laser beams.—N. J. P.

ENVIRONMENT

Breakdown of Chemicals

from a Correspondent

POLLUTION dangers can be reduced and persistence controlled as long as the research effort into the breakdown of man-made chemicals in the environment can keep pace with their usage. There is urgent need for more work in this field with emphasis on greater cooperation between microbiologists, biochemists and chemists. These were the messages to come out of the symposium on microbiological aspects of the breakdown of chemicals in the environment arranged by the Microbiology Group of the Society of Chemical Industry in London on February 3.

The morning session began with a contribution by Dr H. A. Painter (Water Pollution Research Laboratory, Stevenage), who pointed out that the growth of nitrifying microbes requires oxygen and is very susceptible to inhibition by chelating agents, metals and chlorate. He emphasized the need to adopt acceptable and reproducible techniques for obtaining, storing and analysing water samples. Miss S. Beastall and Professor D. E. Hughes (University College, Cardiff) dealt with the microbial breakdown of crude oils. Work at Cardiff had shown that hydrocarbon-oxidizing microbes may comprise 2.5 to 9 per cent of the microbial population of the Bristol Channel. The main factors limiting microbial breakdown of oils are availability of oxygen and mineral nutrients. Methods of combating oil spills are being sought and promising developments include use of biodegradable non-toxic emulsifiers and sinking agents.

Dr J. H. Walsh (University of Manchester Institute of Science and Technology) said that most plastics are not very susceptible to biodegradation and microbial growth often associated with degraded plastic is likely to be on plasticizers or other additives. It was possible, however, that polyurethanes, many of which are degraded by fungi, may be chemically designed so as to exhibit a predictable susceptibility and hence persistence. Mutation or "training" processes enabling microbes to attack plastic polymers seemed unlikely.

In the afternoon session Dr A. J. Willets (University of Exeter) described the degradation of alkyl benzene sulfonate (ABS) surfactants. Many common microorganisms degrade these compounds and use similar metabolic routes, the first and key step being desulfonation followed by oxidation of the alkyl chain and then aromatic ring cleavage. Dr I. Hill (ICI Ltd, Jealott's Hill) pleaded for an examination of pollution of the soil by pesticides. Having described reactions often involved in

pesticide degradation he suggested that chemists should look to the design of biodegradable insecticides. Dr S. J. L. Wright (University of Bath) described the microbial metabolism of phenylamide herbicides. Aniline compounds which are formed as metabolites of such herbicides may in turn either be metabolized or, as in the case of some chloroanilines, condense to form azobenzenes or combine with persistent humic materials. Appreciation of microbiological factors involved in herbicide degradation in certain cases suggested possibilities for both extending and reducing persistence in soil. Several speakers pointed to deficiencies in the "pure-culture" experimental approach to biodegradation problems and suggested that it might be more realistic to use mixed cultures and co-metabolic techniques.

Dr K. Mellanby (Monks Wood Experimental Station) summed up by saying that as long as sufficient effort is directed to understanding the fate of man-made chemicals in the environment, pollution dangers will be minimized and people may continue to enjoy the benefits of their use.

The State of Rhodopsin

Two articles in next Wednesday's *Nature New Biology* (March 15) present new data about the physical state of rhodopsin in the retinal rod membrane. Rhodopsin is a protein, probably of molecular weight 40,000, containing the visual chromophore 11-*cis* retinal. It is known that rods are strongly dichroic, the long axis of the retinal being aligned essentially perpendicularly to the rod axis. In the perpendicular plane, by contrast, there is no measurable dichroism, indicating random rotational orientation. More than ten years ago, Hagins and Jennings found that partial bleaching with polarized light did not result in the generation of dichroism. This was surprising, because the molecules oriented with the chromophore in the direction of polarization should be bleached, leaving those more nearly perpendicular to this direction intact.

P. K. Brown has now confirmed this finding, and he has further shown that if the retinas are first treated with the cross-linking agent, glutaraldehyde, a quite different result is obtained: a high degree of dichroism appears, which increases progressively with the extent of bleaching. In control experiments with the monofunctional formaldehyde no dichroism was generated. These results discriminate between the two obvious explanations of the absence of dichroism after polarized bleaching of untreated retinas, in that they exclude a mechanism involving transfer of excitation energy between chromophores

RIBOSOMES

Contemplating Cores

from our Molecular Biology Correspondent

WHATEVER other marks they may leave on the field, ribosomologists seem rarely to have neglected to contribute their very own nomenclature for ribosomal proteins and factors. This invests the literature on the subject with that curiously impenetrable quality which repels most outsiders. Given patience, however, some new results of no small interest can be quarried from recent work of a number of groups.

Allet (*Europ. J. Biochem.*, **24**, 421; 1972) shows, by analysis of the proteins shed and retained by 50S subunits of *Escherichia coli* ribosomes on treatment with high salt concentrations, that the division into "split" and "core" proteins is in a sense arbitrary. That is to say, there is a spread of effective binding constants, modulated by the conditions. Using lower than customary magnesium concentrations (in the region of millimolar), Allet finds that lithium and caesium chloride produce similar

before the photochemical bleaching event. Such transfer would be unaffected by cross-linking. It may be inferred instead that the rhodopsin molecules are free to rotate about an axis parallel to that of the rod and that they randomize their orientation within the time taken to make the measurements.

This is obviously a result of great general importance, and in the accompanying article Cone describes measurements that show what the rate of the rotational randomization actually is. Using short flashes to produce an intermediate in the bleaching sequence, and measuring the decay of the ensuing dichroism with perpendicular and parallel polarized light, he has been able to measure, by selection of the appropriate wavelength, the relaxation both of the product of partial bleaching and of the residual unchanged rhodopsin. From the exponential decay rates the rotational relaxation time can be extracted, and this comes to about 20 μ s. Assuming the rhodopsin to be a sphere of about 25 Å radius, it is possible to derive an effective viscosity for the membrane medium in which it is located, and the value so determined is such as would be typical for a light oil.

In the light of these data it seems necessary to reconsider the possibility, which had been tentatively discounted by many workers in the membrane field, that a protein of this size could function in favourable cases as a diffusional ion carrier.

results, though differing in the concentration at which they become effective. Examination by acrylamide gel electrophoresis of the proteins in the supernatant and in the pellets after sedimenting the particles through 2 M lithium chloride or 3 M caesium chloride shows that some are present exclusively in one or the other fraction, whereas the remainder are distributed between them.

In principle this effect can be explained in three ways: heterogeneity of the subunits, low specificity in the action of the cations, with only partial extraction of some species, and weak binding, leading to exchange on the core particles. Exchange experiments with labelled cores and added unlabelled proteins or *vice versa* showed that the last and most reasonable of these possibilities is in fact the correct one. The upshot is that under the conditions of these experiments, eleven of the thirty-seven distinguishable proteins are exclusively associated with the cores, nine show no detectable binding, and the rest are distributed between core and supernatant. For the last, effective binding, or at least distribution, constants have been determined. There is evidence that the binding equilibrium is attained at different rates by the different proteins.

The resulting implications for the ribosome assembly process are entirely reasonable, and are consistent with the notion of a small number of very strong primary RNA-protein interaction sites. For the small subunit of *E. coli* ribosomes, Nomura reported that there were no more than two to three such sites, whereas Kurland and his associates, from their binding assays with fractionated proteins, concluded that there are five. The problem has now been re-examined by Garrett, Rak, Daya and Stöffler (*Mol. Gen. Genet.*, **114**, 112; 1972). They use two assay procedures—the co-electrophoresis of an added protein with RNA on acrylamide gels, and elution of protein with the RNA from an agarose column, the protein concentration being measured immunologically with antisera to the individual proteins. The results bear out those of Kurland: five proteins are bound specifically to the 16S RNA, with no competition from the 23S, with 1:1 stoichiometry. One other binds in a non-specific manner with indeterminate stoichiometry. For two of the five binding proteins there is evidence of cooperativity.

The same authors (Stöffler *et al.*, *ibid.*, 125) have studied the interactions of the proteins of the large subunit with their RNA, and here eight of the thirty-four species examined bind specifically at single sites. Six of the eight can be identified as core proteins; there is evidently therefore a small group of

proteins that bind directly with the RNA and are yet displaced from the cores, and the binding of which presumably implicates other core proteins.

An especially interesting member of the group of proteins displaced by salt from the 50S subunit is the highly acidic, alanine-rich A-protein of Möller and co-workers. Möller, Groene, Terhorst and Amons (*Europ. J. Biochem.*, **25**, 5; 1972) now describe the physical properties of this species. Two striking features are that it is present in two modifications, A₁ and A₂, and that, as isolated, it contains two identical polypeptide chains, with a tendency to associate further. The subunit molecular weight as determined by sedimentation equilibrium in guanidine hydrochloride (as well as detergent-gel electrophoresis) is some 12,000. The A₁ and A₂ differ slightly in isoelectric point, but are indistinguishable in terms of amino-acid composition. In all, there are four A polypeptide chains per ribosome (an apparently unique situation among known ribosomal proteins), most probably in the form of two dimers. If the cells are grown in a restrictive medium, the A₂ gives place to A₁. Terhorst, Wittmann-Liebold and

Möller (*ibid.*, 13) show by analysis of tryptic peptides that the two forms differ only in that the N-terminal serine residue is acetylated in A₁—a feature not so far encountered in bacterial proteins. A further unusual characteristic is that one lysine residue is methylated in about half of the chains in both A₁ and A₂.

Earlier work from the same laboratory showed that the A-protein is implicated in translocation, and it is clear what the authors have in mind in drawing cautious attention to the prevalence of ϵ -methyl lysine in contractile proteins. Saporiti and Lengyel (*Biochem. Biophys. Res. Commun.*, **46**, 238; 1972) confirm that a protein from the supernatant (presumably A-protein) is required for one of the two factor-specific GTPase functions that fuel the translocation mechanism. The 50S core is also necessary. (The other GTPase reaction, which involves the ternary complex of aminoacyl-tRNA, GTP and another elongation factor proceeds in the presence of the 50S core alone, without any supernatant proteins.) Evidently a range of protein interactions within the ribosome is involved in propelling it along the messenger.

Muscle Preservation at Low Temperatures

In order to preserve biological material for long periods of time, it is necessary to store it at very low temperatures, well below 0° C. The freezing and subsequent thawing processes can easily disrupt both the structure and function of the materials so that methods have been evolved whereby certain non-electrolytes, such as glycerol or dimethyl sulphate (DMSO), which considerably lower the freezing point are added to the bathing medium. Although preservation is improved by these methods, there is still considerable disruption compared with fresh material. In next Wednesday's *Nature New Biology* (March 15), Elford and Walter describe a method whereby the structure and function of smooth (guinea-pig) muscle preserved at -79° C are almost as good as those of the freshly dissected muscle.

The new aspect of Elford and Walter's method is that they use bathing media with high potassium levels which resemble the intracellular fluid; all previous methods have used Krebs-based media with a high sodium content resembling the extracellular fluid. By use of such media, Elford and Walter hoped to reduce ionic imbalances occurring during cooling. Three different potassium-rich media buffered with N-tris (hydroxymethyl)-methyl-2-amino-ethanesulphate (TES), piperazine-NN'-bis-2-ethanesulphonate (PIPES) and glycerophosphate respectively were

used. It was hoped that the anions provided by the buffers would remain extracellular, thereby maintaining as normal an internal environment as possible. Strips of taenia coli muscles in each of the above three media, and in a standard Krebs medium, were subjected by stages to increasing concentrations of DMSO at decreasing temperatures for a few hours, and then stored overnight at -79° C in 60 per cent DMSO media. The muscles were rewarmed by similar stages, and their contractile responses to histamine and their structures in the electron microscope were compared with those of a control, freshly dissected muscle.

The improved performance of muscles in the potassium-rich solutions was very obvious: whereas the mean maximum tension of muscles in the Krebs-based medium was only 35.5 per cent of the control, the corresponding values in the three potassium-rich solutions were around 80 per cent, the PIPES-buffered media being best at 86.3 per cent.

Elford and Walter are unable to conclude at present whether the improvement of preservation in their media is attributable to the increased potassium *per se* or to the large impermeant anions. Be that as it may, the method represents a promising new approach; it would be interesting to see whether it can also improve the preservation of other biological materials.

GENE EXPRESSION

Switching Transcription

from our Cell Biology Correspondent

THREE weeks ago *Nature* (235, 329 and 360; 1972) published Haseltine's report that, at least in the conditions he uses, psi factor is not required specifically for the transcription *in vitro* of the ribosomal RNA genes of *Escherichia coli* by *E. coli* RNA polymerase. This finding contradicts the results of Travers and his colleagues (*Nature*, 228, 748; 1970) who have claimed that psi factor is required for the transcription of ribosomal RNA genes *in vitro*. The reasons for this discrepancy are as yet obscure; they may be trivial and stem from small differences in the incubation media used but they may be of biological significance.

That *E. coli* RNA polymerase holoenzyme ($\alpha_3\beta\beta'\sigma$) can synthesize ribosomal RNA *in vitro* in the absence of psi factor cannot, however, be disputed and in the current issue of the *Proceedings of the US National Academy of Sciences* (69, 407; 1972) Hussey, Pero, Shorestein and Losick report that RNA polymerase from vegetative cells of *Bacillus subtilis* also transcribes *in vitro* the heavy strand of *B. subtilis* DNA to yield an RNA which in hybridization experiments competes with *B. subtilis* ribosomal RNA made *in vivo*. Indeed, highly purified *B. subtilis* polymerase, lacking a psi factor, apparently preferentially synthesizes ribosomal RNA, for this RNA comprises 8 per cent of the total RNA made *in vitro* even though the ribosomal RNA genes comprise only about 0.4 per cent of the bacterial genome. Moreover, sigma factor is required for the transcription *in vitro* of the ribosomal RNA genes.

Hussey *et al.* also report that RNA polymerase from stationary phase cells of a mutant strain of *B. subtilis*, *rfr* 10, which cannot sporulate, retains the capacity to transcribe ribosomal RNA genes *in vitro* whereas enzyme from wild type cells undergoing sporulation synthesizes very little ribosomal RNA *in vitro*. Losick's group have shown that during sporulation the polymerase loses sigma factor and the β subunit is modified and at the same time synthesis of ribosomal RNA is switched off. It is tempting therefore to conclude that these changes in the polymerase are responsible not only for the cessation of synthesis of ribosomal RNA but also for the initiation of synthesis of RNA species unique to sporulating cells.

B. subtilis has attracted attention not least because the process of sporulation has several analogies to cell differentiation in higher organisms, and *Caulobacter crescentus* is another bacterium which seems destined to be increasingly

studied as a model of developmental systems. *Caulobacter* has a curious life cycle—it exists in a stalked-cell form and in a motile swarmer cell form. The stalked cells divide repeatedly to produce a daughter stalk cell and a swarmer cell which, before it can divide, has to convert itself into the stalked form.

Using synchronous cultures of *Caulobacter*, Newton (*ibid.*, 447) has investigated the effect of rifampin on the loss of motility, initiation of DNA replication and cell division during the *Caulobacter* life cycle in an attempt to gain some indications of the stages at which changes in the pattern of transcription may be crucial. As anticipated he finds that progression through the life cycle depends on RNA synthesis,

but some events are sensitive to prior exposure to rifampin. Loss of motility by swarmer cells, for example, occurs some 40–45 min after incubation is started, but it can only be blocked by rifampin during the first 15 min of incubation; thereafter it becomes insensitive to the drug. By contrast, formation of the stalk which occurs after about 60 min can be blocked by adding rifampin at any time during the first 50 min of incubation.

Results such as these strongly suggest that during the life cycle of *Caulobacter* differential gene expression is at least in part achieved by regulatory mechanisms acting at the level of transcription. No doubt it will not be long before the structure and specificity of *Caulobacter* RNA polymerase will be reported.

Cosmic Rays and Scaling

COSMIC-RAY physics has long been a borderland subject, contributing sometimes to astrophysics, sometimes to the physics of elementary particles. Two decades ago, cosmic-ray workers were the pioneers in studying meson and baryon spectra, and it is conceivable that they will yet cap all by pinning down the elusive quark. At present, however, the flow of information is mostly in the other direction. Accurate cross-sections measured in accelerator laboratories are used to draw conclusions about astrophysics from cosmic-ray measurements, and nobody waits more eagerly than do cosmic-ray physicists for news from Serpukhov, CERN and Batavia.

Unfortunately the high-energy end of the primary cosmic-ray spectrum lies more than six orders of magnitude above the highest accelerator energy yet envisaged. For many cosmic-ray calculations there is no option but to extrapolate—or guess—according to what seems to be the most reasonable assumptions. This applies in particular to the calculation of secondary processes taking place in the atmosphere after the entry of the primary cosmic-ray particles. If the interactions were thoroughly understood it would be possible to infer the detailed composition of the primary radiation from observations of the secondary particles at the Earth's surface. This cannot yet be done.

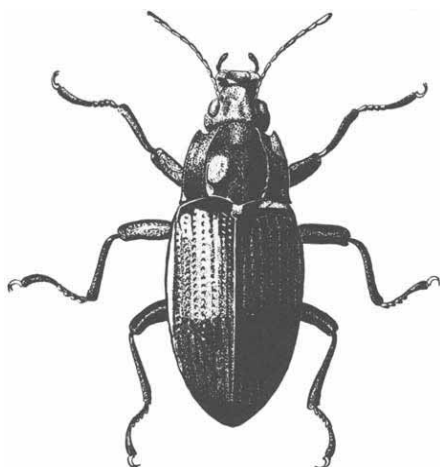
The favourite procedure in the past few years has been to suppose that most secondary particles produced in nucleon-nucleon collisions are pions, that their number varies as (available energy)¹, and that their energy spectrum is given by the formula proposed by Cocconi, Koester and Perkins (CKP) in 1963 to describe the experimental data at 20 GeV. Sometimes a certain proportion of excited baryons is incor-

porated in the model, the baryon decay providing a few mesons of higher energy. A new way of extrapolating the accelerator data to higher energies has been suggested recently by Feynman, with his hypothesis of "scaling". One consequence of scaling would be that the number of secondary particles carrying a significant fraction of the interaction energy increases only slightly with increasing energy. The appearance of this alternative model allows the sensitivity of astrophysical conclusions to be checked relative to the choice of model. Can the nature of the primary cosmic radiation really be inferred from what is seen of the secondaries at ground level?

In next Monday's *Nature Physical Science* (March 13), Wdowczyk and Wolfendale consider the two theoretical models, particularly in relation to the primary particles of energy $\sim 10^{14}$ eV. They show that there is a significant difference in the number of multiple muon events observable underground on the two hypotheses. The experimental data obtained by Keuffel and his colleagues at Utah may be explained either on the traditional model—CKP and (energy)¹—with a primary cosmic-ray beam consisting principally of protons, or it may be explained on the scaling model, provided that the primary particles of energy are supposed to have mass number $A \sim 5$.

Wdowczyk and Wolfendale mention some objections to this high mass number, but cautiously avoid committing themselves to a preference for either hypothesis. They do suggest, however, that the scaling hypothesis might require primary particles at 10^{18} eV to have very large masses indeed, $A \sim 50$, a conclusion very different from the conclusions they and others have reached in the past.

FRESHWATER BIOLOGY

British Riffle Beetles

THE Elminthidae, or riffle beetles, are a family of freshwater beetles in the superfamily Dryopoidea. In the past decade there has been much difference of opinion in the literature over the systematics of the Elminthidae so that British biologists will be glad to have D. G. Holland's new guide to the members of the family found in British rivers and lakes (*A Key to the Larvae, Pupae and Adults of the British Species of Elminthidae*, Freshwater Biological Association (Scientific Publication No. 26), £0.40). This illustration, taken from the key, is of *Limnius volckmari*, the largest common British elminthid which is found under stones in streams and rivers. It ranges in length from 2.85 to 3.20 mm.

CANCER RESEARCH

Chemical Oncogenesis

from a Correspondent

CHASING carcinogens into cells and seeking them out as environmental hazards are recognized as proper occupations for cancer research workers. This and more was learnt at the seventh meeting in the series on principles of clinical and experimental oncology at the British Museum (Natural History) on February 21. Dr P. Brookes (Institute of Cancer Research) presented the viewpoint of experimental carcinogenesis, and Professor R. A. M. Case (Institute of Cancer Research) discussed the epidemiological angle.

Dr Brookes concentrated on a study of the metabolism and mechanism of action of known carcinogens. In addition to such polycyclic hydrocarbons as 1,2,5,6-dimethylbenzanthracene, a wide range of chemical compounds including both synthetic and naturally occurring materials has been shown to be carcinogenic. The variety of such materials makes it difficult to understand the nature of induced malignant change. The alkylating agents have been studied

in great detail both for their carcinogenic and cytotoxic properties, and it seems that alkylation of DNA is the reaction most likely to be correlated with a biological effect such as carcinogenic or mutational change. It has been established that there are several possible products of alkylation of constituents of DNA and to a limited extent it is possible to ascertain which of these are the most significant in relation to a particular biological effect. The innate complexity of mammalian cells, and inadequate knowledge of the arrangement and operation of their genetic materials, are likely to remain barriers to progress for some time.

Dr Brookes said that the study of repair mechanisms had increased understanding of mammalian cell biology and he felt it was significant that patients with xeroderma pigmentosa seem to lack one of the nucleic acid repair enzymes; the inference is that the high incidence of squamous cell carcinoma in these patients is associated with failure to repair damage to the genetic material induced by ultraviolet light.

Professor Case distinguished occupational from recreational hazards and identified β -naphthylamine, exposure to which can lead to bladder cancer, as an example of the first, and smoking as an example of the second. In relation to occupational hazards, epidemiologists could classify hazards as those which are recognized and which are subject to legislation, those which are suspect and which should be the subject of experiments, and unrecognized hazards. Hazards in the second category, in which Professor Case is particularly interested, are in some ways to be thought of as *sub judice* and therefore not appropriate for public discussion. Professor Case illustrated the difficulties encountered in giving advice about carcinogenic hazards and emphasized that success in reducing occupational exposures depends on goodwill at all levels of industry.

GENETICS

Using Somatic Cells

from a Correspondent

SOMATIC cell geneticists face the problem that their tissue culture lines are not naturally haploid. Indeed many cell lines have considerably more chromosomes than the diploid number and, because most of the mutants which one would want to isolate are recessive, the likelihood of inducing mutants with the appropriate mutation in all the gene copies seems slim. And this ignores the even thornier situation which would arise if many structural genes were tandemly duplicated.

One way round this might be to isolate haploid cell lines. This has

already been achieved by Freed and Mezger-Freed in the frog *Rana pipiens* (*Proc. US Nat. Acad. Sci.*, **65**, 337; 1970) although this line seems to have certain disadvantages, not the least of which is that there is very little classical genetics of the frog. Some groups have tried to induce mutants in cell lines; the drug resistant variants isolated so successfully by Littlefield (*Proc. US Nat. Acad. Sci.*, **50**, 568; 1963) have already become standard laboratory reagents for isolating cell-fusion hybrids or tracking chromosome loss, but what are needed most urgently are conditional lethal mutants that are available so abundantly in other fields.

Naha showed in 1969 (*Nature*, **223**, 1380; 1969) that it was possible successfully to isolate temperature sensitive clones from established tissue culture lines, but his observation seems to have gone almost unnoticed. Interest now seems to be picking up, however, and several groups are selecting temperature sensitive cell variants. At the Ontario Cancer Institute Thompson *et al.* have isolated temperature sensitive variants of mouse L cells (and they do not come much more aneuploid than that) by first treating the cells with the mutagen nitrosoguanidine and then either selecting with cytosine arabinoside or ^3H -thymidine to kill those cells which can grow at the non-permissive temperature or simply by plating out the mutagenized cells and testing directly for temperature sensitivity of the clones (*J. Cell Physiol.*, **78**, 431; 1971). By this last method these authors show that out of 1,310 separate clones tested, 18 were temperature sensitive for growth—a staggeringly high frequency of 6×10^{-3} . Thompson *et al.* go on to describe some of the properties of their variants such as their patterns of uptake of ^3H -thymidine, ^3H -uridine and ^3H -leucine and their plating efficiency, and it is clear that a wide range of phenotypes has been isolated.

One awkward fact is the very high rate at which temperature insensitive revertants appear in cultures of the variants; rates as high as 10^{-4} are not uncommon. It remains to be seen therefore just how useful these types of cell will be for biochemical studies and, indeed, in view of the doubts raised by Harris's work (*J. Cell Physiol.*, **78**, 177; 1971) and by others the question arises whether these temperature sensitive variants are structural mutations of the expected kind at all. Why are they found at such a high frequency, and why do they revert so easily? The answers to these questions will no doubt not be easy to obtain, but it is clear that somatic cell genetics is about to enter a new phase where a wealth of phenotypic variants are available for study.

Teacher Attitudes to Projects in A-Level Engineering Science

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In this article a comparison is made between the objectives of coursework in A-level engineering science, as published by the Joint Matriculation Board, and those considered important by the teachers who have been directly involved.

ALTHOUGH the concern which senior education officials continue to express about the failure of so-called "bright" children to enter industry¹ may be questioned², the welcome fact is that the apparent shortage of qualified technologists has led to important changes in opinion about the value of technological studies in schools³ since the publication of the Page report⁴. An undoubted influence on this debate was provided by the many studies of pupil attitudes that have been reported⁵⁻⁷. The importance of the teacher was recognized but there have only been one or two investigations of teacher attitudes to engineering and technological studies⁸ apart from the Page enquiry. Criticisms of teachers—such as those in a recent National Economic Development Office (NEDO) report on manpower—without resort to the evidence seem somewhat unfair⁹. They merely serve to justify the criticisms of Gannicott and Blaug¹⁰ that such committees are motivated from self-interest. The significance of teacher attitudes increases as changes are made in the curriculum and the successful adoption of engineering subjects in schools depends very much on the willingness of teachers to experiment and innovate. The extent to which innovations are successful is likely to depend more on the teacher and his resources (that is, adaptability, time, ideas, facilities and so on) than on student abilities to pursue new-style learning. The willingness to change was undoubtedly aided by the Nuffield projects in school science.

A-Level Engineering Science

In 1967, 29 students in five schools embarked on engineering science, a Joint Matriculation Board (JMB) equivalent to physics A-level¹¹, in the knowledge that universities would accept this equivalent with suitable grades as a means of university entry. Since then some 270 students have taken this examination and forty-three schools (including three technical colleges) have offered courses for this subject. As well as a new approach to the syllabus and an examination which was considerably different in structure from the traditional style, radical innovations were implemented in coursework which required the completion of a 50 h project and accompanying dissertation, and four experimental investiga-

tions of up to 12 h duration, subsequently reduced to three. Various aspects of the course have been evaluated. Most recently, teacher attitudes to the projects have been obtained and it is these which are the subject of this article.

A comparison of JMB published coursework objectives¹¹ was made with an inventory of objectives derived by one of us (D. A. H.) from published sources. Its purpose was to obtain the attitudes of teachers to projects of any kind. Because the published JMB objectives could be related to the inventory either directly or by inference and because the inventory had been the subject of a satisfactory pilot investigation, it was distributed to the teachers in the forty-three schools without modification. An open-ended question was included in order to obtain independent comments on JMB coursework. The purpose of this particular enquiry was to throw some light on the extent to which the pressure of coursework was leading to dissatisfaction with the project.

Teachers in thirty-three schools (78%) rated twenty-nine possible aims of projects for their effectiveness and their importance. The results are represented in Fig. 1 which relates effectiveness to importance. The criteria for the effectiveness of each item are weighted as follows: highly effective, +3; effective, +2; of little effect, +1; ineffective, 0; of adverse effect, -2. The maximum score for effectiveness is 96. The weightings were derived from the judgments of sixteen teachers not included in the sample. Importance was scaled for very important, of some importance and of no importance. The illustration shows effectiveness as a function of the degree of importance, in rank order of the scores for effectiveness. The importance scale has not been weighted. As would be expected, teacher views of effectiveness and importance turn out to be closely related.

Table 1 shows the responses to a separate question which asked the teachers to indicate the six most important aims

Table 1 The Six Most Important Aims and Objectives in Order of Number of Responses

Rank order	Objectives	No. of responses
1	Increasing self reliance by independent work	19
2	Increasing decision-making ability	15
3	Training pupils to find out for themselves	15
4	Increasing readiness to accept responsibility	14
5	Assessing those abilities not revealed by traditional examinations	14
6	Improving the ability to communicate	13
7	Developing creativity	11
8	Giving pupils a sense of involvement	9
9	Improving problem solving abilities	8

All these responses scored 25% or more of the total.

and objectives. Comparison of these with the first JMB statement of objectives and with the 1971 JMB published statement of assessment procedures for engineering science at A-level¹¹ shows a discrepancy between intention and practice in that, whereas seven of the nine objectives are clearly catered for by the assessment procedure, only four may be related directly to the statement of objectives. This may be accounted for by the influence of the cognitive skills listed in the *Taxonomy of Educational Objectives*¹². Teacher perception of statements of objectives on the one hand, and the methods of assessment on the other, is probably not without significance in terms of the effectiveness with which the objectives communicate the aims of the course to those not closely connected with the development.

It seems significant that none of the objectives listed relate specifically to the pursuit of a vocation in a particular technology. They could equally well be applied to projects in the humanities. Indeed, as a means of inclining students to pursue technology as a career, the findings of this enquiry show teachers to have little sympathy with the view that projects had this effect or, for that matter, should have this aim. It is also surprising that projects are not thought to be highly important or effective in generating interest. There is, however, a suggestion that this view may be in contrast with those of pupils in the same schools. The results of pupil interviews have yet to be analysed. Most students taking this subject intend to pursue engineering in one way or another.

Contrary to the commonly held view that performance in projects will help some poor students to increase their

mark¹³, teachers of JMB engineering science are emphatic in rejecting the idea of project work as being an alternative route for the academically weaker pupil. It must be remembered that this view is based on experience of actual moderation and the correlation of their student ratings with final performance. Teachers rate communication as important but doubt is expressed about the effectiveness of projects in developing this skill in spite of the fact that pupils complete a dissertation and are also interviewed by the moderators.

Open-ended Questions

To enable teachers to express their opinions, and in the hope that some reasons for the choice of objectives would emerge, two open-ended questions were included. One related to JMB coursework as a whole, the other asked teachers to respond to the hypothetical situation of advising other teachers. It said "A school, similar to your own, is considering the introduction of project work into one of its sixth-form science courses. The master concerned is unsure whether the staff and facilities available will prove suitable, whether projects are too difficult to supervise and whether project work is really worthwhile anyway. Please indicate briefly, from your experience of project work, what would be your advice to him".

If it is assumed that a statement of this kind is likely to cause relatively cautious stances to be adopted, the overall impression remains that these teachers like projects. Analysis of the responses shows that seven were strongly in

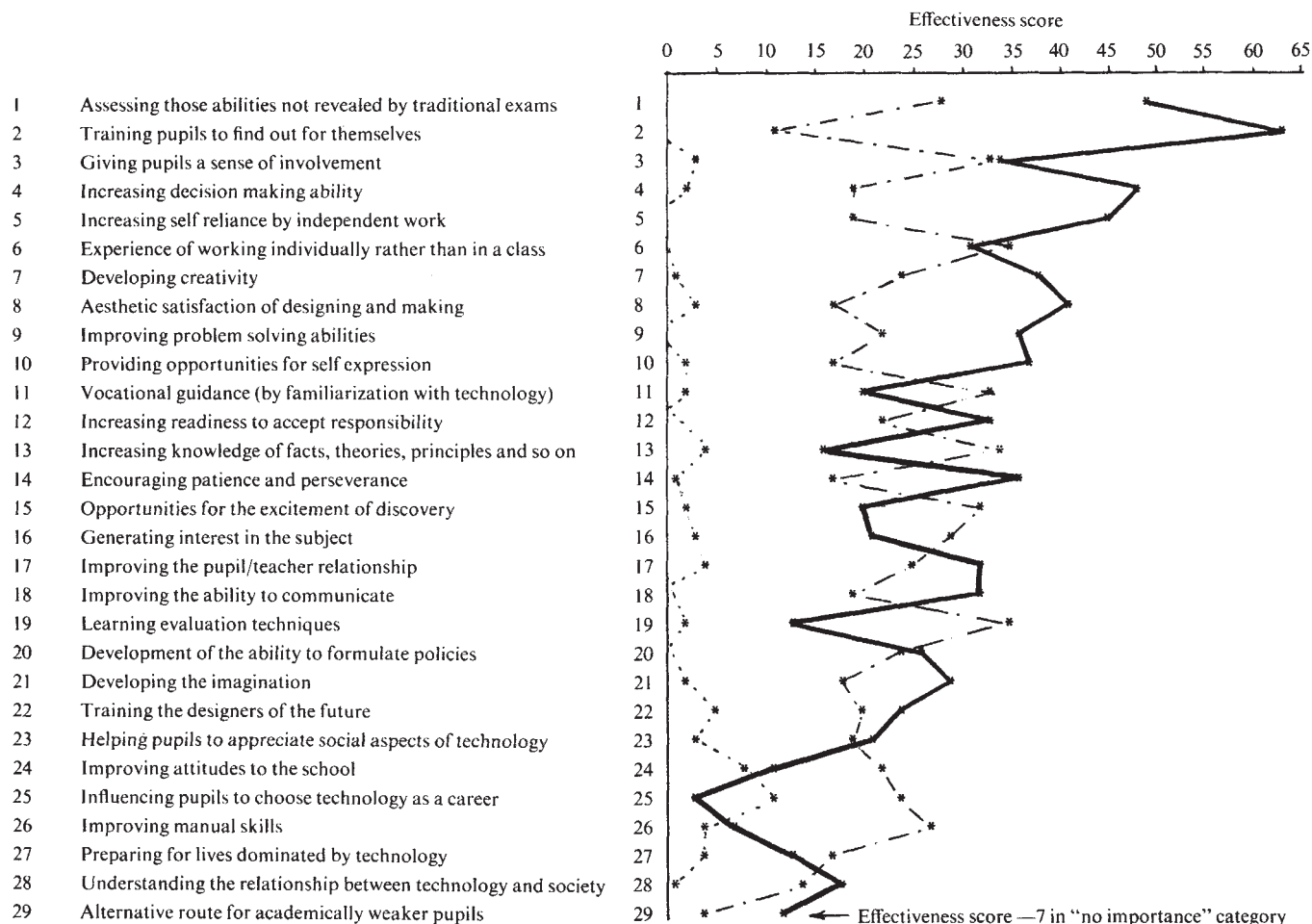


Fig. 1 Teacher ratings of the effectiveness of project work. The effectiveness scores are weighted as explained in the text. As well as rating its effectiveness, teachers were asked to indicate what importance they attached to each objective. —, Effectiveness scores in the category "very important"; ---, effectiveness scores in the category "of some importance"; ····, effectiveness scores in the category "of no importance". The objectives are in rank order of effectiveness.

favour of project work, four were favourably inclined, twelve gave the impression of being in favour, two were anti-project and the remaining six did not write anything from which an attitude could be detected.

The teachers were generally of the opinion that projects engendered enthusiasm and, as a consequence, more work from students than would normally be expected. The pupils undertook wider reading and enjoyed the relative freedom of thought and movement; some, however, did not find project work stimulating.

School teachers evidently associate projects with the aims traditionally associated with grammar school education, that is, the development of "the whole man", for the objectives given most importance relate to personality traits as much as to the acquisition of cognitive skills. Problem solving is rated ninth. It is interesting to relate these views of the objectives of projects to those of personnel and training officers in another enquiry¹⁴, 30% of whom thought that personality was as important a factor in the competition between individuals with widely different technical qualifications as ability. Almost all of those interviewed gave some credence to the importance of personality in the selection process.

Project work, teachers reported, developed important aspects of character and ability that are normally ignored in teaching for examinations. Pupils not only learn a tremendous amount of knowledge that is only remotely connected with the examinations but acquire interesting experience of the excitement and frustration that will inevitably be encountered in later life. Projects encourage initiative, independence, ability to work on their own, confidence (which also seems to be generated by the interviews with the moderators), the ability to use a library and the provision of knowledge of real problems in real situations, to quote but some of the comments.

Nevertheless, as answers to the statement showed, teacher enthusiasm for projects was tempered by reality. For example, "pupils must be encouraged but they must also be allowed to proceed at their own pace which is sometimes desperately slow". More important perhaps were the views that projects could not be adequately supervised if there were more than eight to ten students a teacher. Project work should not be isolated from other resources (for example, technical colleges and industry). The utilization of such resources "spread the load" and reduced the work involvement and excessive consumption of time. Some JMB projects had been completely undertaken in industry. It was suggested that separate rooms specially designed for project work¹⁵ were necessary. The idea that shortage of equipment could very often be overcome by the imaginative use of existing equipment completes this summary of responses to the open-ended questions.

It should be mentioned that sixteen of the teachers in the sample had engineering qualifications. This compares with the 33% of teachers with engineering qualifications in the very much larger sample of schools taken by Page in his enquiry in 1964. Some of these schools carried out a deliberate policy of recruitment for staff with engineering backgrounds and/or qualifications.

An impression which persists is that the teachers perceive projects in a different light from those who developed the written statements of objectives, and whose thinking was obviously conditioned by the syllabus requirement to introduce the applications of science through projects into schools. The influence of pupils and teachers on the subsequent activity is to be seen in the acceptance of the board of several projects with social and/or behavioural content (for example, studies of local traffic systems; an operational research study of a hospital ward; human reaction times).

The data collected so far do not by themselves lead to any positive conclusions about the loading of coursework because they do not take into account the influence on learning of

the three experimental investigations. Questions need to be asked about the effect of these investigations on the transfer of skills and their acquisition as between practical work in different disciplines (for example, electronic and mechanical). It seems certain at this stage that teachers and students often find that the investigations provide a useful preparation for the full undertaking of a project. Some respondents went as far as to say that pupils should have opportunities to become familiar with the techniques required for project work well before the sixth form. Furthermore, the "reality" of the project at this age evidently lies in the activity itself and not in its usefulness of replication of engineering situations. Inspection of the projects confirms the value of McDonald's distinction¹⁶ between creativity and originality that "creative is the label we apply to the products of another person's originality", for even in projects that are essentially replication (for example, engine test beds for use in the school) it is possible to find originality (that is, "behaviour which occurs relatively infrequently, is uncommon under given conditions, and is relevant to those conditions"¹⁷).

Complaints that projects cause students to spend more time on that activity than on their other subjects are met by the argument, first, that the time allowance of 50 h, although flexible, is nevertheless a not inconsiderable restraint and, second, that it is surely up to teachers of the other subjects to find ways of stimulating pupil interest. In any case, as enquiries have shown, the balancing of effort as between different activities in universities¹⁸ is a considerable problem for first year students and sixth form activities of this kind might be a helpful preparation.

There are several answers to criticisms of the loading of coursework. One of them is to alter the relative proportion of marks allocated to coursework—20% at present; but because the correlation between A-level and university performance is regarded by selectors as being significant, it is necessary to adopt rigorous procedures for the activity and its assessment when the relative marks for coursework are high. Teachers may feel that the proportion is not adequate for the rigour demanded. In a more recent enquiry carried out by one of us (J. H.), almost the same group of teachers were asked which of three marks they considered to be the most appropriate score for coursework as outlined in the present regulations. Twelve (42%) voted for the present mark of 20%, fourteen (50%) suggested 25%, and two (7%) were in favour of 30%.

We thank the Joint Matriculation Board and the teachers for their help in the pursuit of this enquiry. One of us (D. A. H.) thanks the Social Science Research Council for a studentship.

¹ Haines, K., *Light Engineering*, June 1971.

² Entwistle, N. J., *New Academic*, 1, No. 1.

³ *Project Technology*, Nos. 1 to 18 (Schools Council, 1971).

⁴ Page, G. T., *Engineering Among the Schools* (Institution of Mechanical Engineers, 1965).

⁵ Hudson, L., *Nature*, 196, 601 (1962).

⁶ Hutchings, D. G., *The Sixth Former and Technology* (Oxford University Department of Education, 1962).

⁷ Jones, G., *New Scientist* (January 31, 1963).

⁸ *Qualified Manpower in the Electronics Industry* (NEDO, 1971).

⁹ Heywood, J., Mash, V., and Pollitt, J., *Lancaster Studies in Higher Education*, No. 1 (April 1966).

¹⁰ Gannicott, K. G., and Blaug, M., *Higher Education Review*, 2, 65 (1969).

¹¹ *Syllabus and Notes for the Guidance of Schools on Engineering Science ('A' level)* (Joint Matriculation Board, 1971).

¹² Bloom, B., et al., *The Taxonomy of Educational Objectives*, 1 (Longmans Green, 1964).

¹³ Taylor, L. J., *Project Technology*, Occasional paper 2 (Schools Council, 1969).

¹⁴ Heywood, J., thesis, Univ. Lancaster (1969).

¹⁵ Heywood, J., thesis (College of Preceptors, 1963).

¹⁶ McDonald, F., *Educational Psychology* (Wadsworth, 1968).

¹⁷ Maltzman, I., et al., *Psychological Monographs*, No. 493 (1960).

¹⁸ Heywood, J., *Universities Quarterly*, 25, 189 (1971).

Spread of Spruce (*Picea abies* (L.) Karst) in Fennoscandia and Possible Climatic Implications

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The stepwise spread of spruce from east to west was probably determined by periodic fluctuations in the climate.

RADIOCARBON datings for the relevant horizons in pollen diagrams have confirmed, during the past 10 yr^{1,2}, the earlier conclusion^{3,4} that the spruce spread into Fennoscandia from the east during the post-glacial period. Some confusion has arisen, however, from a failure to separate the stages involved: first, the immigration and establishment of local small stands of trees in microclimatically favourable habitats, a process perhaps delayed in some regions by other ecological factors until the onset of interference of the local vegetation by pre-historic farming activities⁵; and second, the spread *sensu strictu* during which the spruce expanded from these bridgeheads to form a common, or dominant, component of the natural forests in that particular region as and when the regional climate became suitable. The two stages may be a few centuries or millennia apart in time, in different regions. The second of the two stages, itself, seems to have taken place, in the main, stepwise from east to west in Fennoscandia.

The criteria used to define the second stage are: start of rise—the point in time at which the spruce pollen curve (as % total tree pollen) begins to rise, clearly and unbrokenly, from earlier sporadic or continuous “tail” values of 1% or less, due allowance being made for the type of deposit, terrestrial or limnic, and the regional vegetation cover at that time at that altitude; mid-rise—literally midway in the rising curve and, excepting limnic deposits from large lake-basins, pollen values of at least 8–12%; finish of rise—the culmination of the initial major increase in spruce pollen, values from 20–40%, in limnic deposits often remaining steady at 10–20%. The relative course of the spruce curve forms the basis, however, and no claim is made for interpreting minor percentual changes in pollen values in terms of presence/absence of trees, locally or regionally, until more is known about the true comparability of sites.

Local Establishment

The evidence for the first stage, local establishment, is three-fold. First, the presence in the pollen diagrams from scattered lowland sites in all three countries of short lived peaks of spruce pollen (5–10% values for two or more consecutive samples) from horizons one or more metres below the horizon at which the second stage is evidenced, and which are not suspect on the grounds of occurring at the transition from limnic to telmatic deposits or of being secondarily derived from interglacial deposits. At several sites there are ¹⁴C dates for these horizons, for example, one in Trøndelag of 2350 bc. Second, sparse but definite macrofossil finds of spruce cones, cone-scales, needles and twigs, either related to ¹⁴C dated deposits (East Finland) or from unequivocal archaeological contexts (Central Sweden), which are at least 1,000 yr earlier than

the regional spread of spruce (stage 2) in these areas. Third, for the Trøndelag area only at present⁶, place-name evidence for the presence of local stands of spruce by AD 600 or earlier.

Regional Expansion

A closer examination⁷ of the published radiocarbon dates for the second stage, as evidenced in the published pollen diagrams, together with recent unpublished results from the Botanical Institute of Trondheim University, for the Trøndelag region of Norway into which spruce immigrated early (2–3000 bc) yet spread (expanded) late (twelfth to fifteenth centuries AD), shows a clustering of the dates in certain epochs (Fig. 1). The greater spread of the dates for the regional expansion of the spruce after 200 bc is understandable because these datings to some extent derive from areas in which the spruce was approaching its limits as we find them in the historic period (sixteenth to nineteenth centuries). In some parts the winter climate may already have turned favourable, but competition from the beech (*Fagus sylvatica* L.) for similar habitats, or from the pine (*Pinus sylvestris* L.) in areas exposed to summer drought, edaphic and/or climatic, may have hindered any large-scale spruce expansion until human interference with the forests swung the balance, or until a change in summer conditions ensued.

Unfortunately there are at present no radiocarbon dates for the immigration or spread of spruce in southern and western Norway, though pollen analyses support the view that in the latter area both occurred during historic time⁸.

Climatic Distribution

I consider that the distribution of spruce is primarily climatically determined; the important parameters being a high enough summer temperature for seed maturation, a sufficiently low and unbroken winter temperature for seed and seedling survival, and favourable rainfall, or local edaphic conditions, during the early summer for seedling establishment and growth⁹. Once established, the longevity of spruce makes subsequent survival through periods of unfavourable climate, over 2–300 yr or more, perfectly feasible, as evidenced by the satisfactory growth of spruce in Denmark, western Norway and Britain when planted out as 3 yr old seedlings, though this is complicated by the introduction of spruce races of differing provenance.

My interpretation of the evidence in Fig. 1 is that during certain epochs, at about 900 yr intervals, suitable climatic conditions for the spread of spruce occurred sufficiently frequently for regional success. The prerequisite fall in winter temperature seems to have extended its domain gradually further and further westwards during successive epochs, and concomitantly presumably to lower altitudes in mountain areas as well, and the spread was finalized by cooler and/or wetter summer conditions. An indication of the sequence of epochs is indicated, beside the plotted dates, which mainly refer to the period midway during the spruce spread, and a correlation with the meteorologists' alternation of periods of pre-

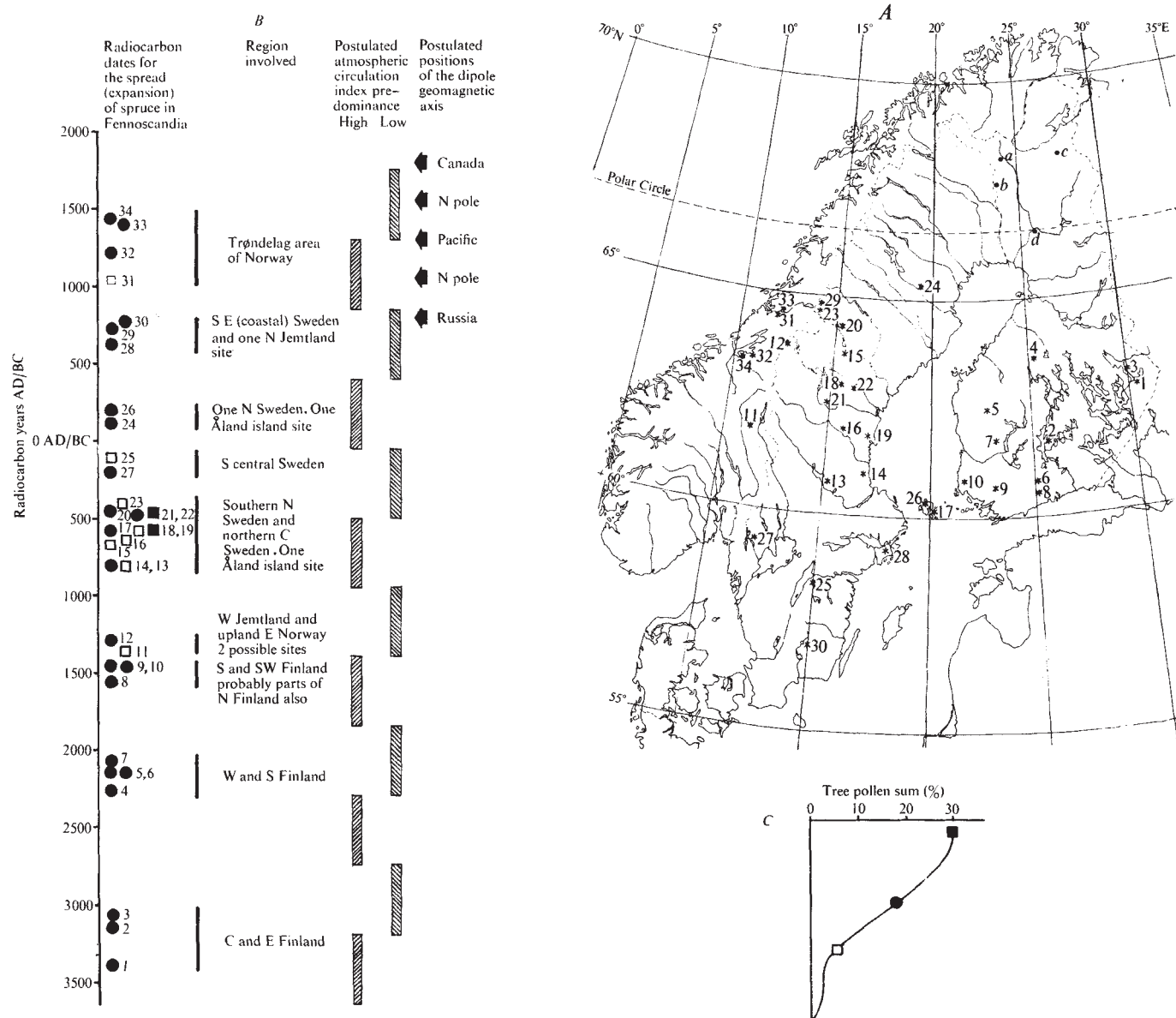


Fig. 1 A, Sketch map showing the positions of dated sites. ●, Omitted from B because the lack of a published diagram makes it impossible to check on dated phase of second stage, or stratigraphy (otherwise they fit the ¹⁴C clusters quite well). a, 1410 BC (mid-rise?); b, 1500 BC (mid-rise?); c, 1650 BC (mid-rise?); d, 2400 BC (mid-rise?). B, Stages of spread of spruce. □, Start of spread; ●, mid-way; ■, finish of spread. C, *Picea* pollen curve (idealized) showing relative positions of ¹⁴C-dated samples.

dominant high or low index atmospheric circulation patterns is suggested¹⁰. The correlation seems likely to be strengthened rather than weakened by the various correction schemes proposed for bringing radiocarbon years into line with Sun years^{11,12}.

A simple alternation scheme does not seem to be sufficiently plausible, however. Three variables, at least, are concerned: (a) changes in the circulation index and related shifts in cyclone tracks; (b) changes in the overall strength of the atmospheric circulation; (c) a long-term change in air/sea temperatures, which has been downward since the climatological optimum about 4000 BC. As a possible cause of (a), I suggest that the apparent correlation in time between the known climatic changes of the historical period¹³ and the positional changes of the dipole geomagnetic field^{14,15} provides a clue, while admitting that, on the basis of the three dates presented for the latter, the cycle length is 500, not 450, yr. If a geomagnetic skewing effect on the atmospheric circulation could be proven, the centres involved being Canada east of the Rockies (AD 1800), the mid-Pacific (AD 1300), and Russia just east of the Urals (AD 800), all points related to common positions of upper air troughs and ridges, then we might have an explanation for the observed facts^{16,17} that the main periods of post-

glacial glacier growth and peat-bog growth in the northern hemisphere have occurred at longer and somewhat more irregular intervals than could be accounted for by previous cyclical theories of climatic change. As a mere botanist I appeal to the meteorologists for help here.

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- 1 Aario, R., *Bull. Comm. Géol. Finlande*, **218**, 215 (1965).
- 2 Aartolahti, T., *Ann. Bot. Fenn.*, **3**, 368 (1966).
- 3 Gløersen, A. T., *Norske Forstforen. Aarb.*, **1884**, 40 (1884).
- 4 Sernander, R., *Engler's Bot. J.*, **15**, 1 (1892).
- 5 Markgraf, V., *Nature*, **228**, 249 (1970).
- 6 Tallantire, P. A., *Namn Och Bygd*, **58**, 161 (1971).
- 7 Tallantire, P. A., *Norweg. J. Bot.* (in the press).
- 8 Faegri, K., *Univ. Bergen Aarb. Math.-Naturvid. rekke*, **1** (1949).
- 9 Hintikka, V., *Ann. Bot. Soc. "Vanamo"*, **34** (5), 1 (1963).
- 10 Lamb, H. H., in *World Survey of Climatology* (edit. by Flohn, H.), **2**, 173 (Elsevier, Amsterdam, 1969).
- 11 Stuiver, M., *Nature*, **228**, 454 (1970).
- 12 Tauber, H., *Aarb. Nord. Oldk. Hist.*, **1970**, 120 (1971).
- 13 Lamb, H. H., *Palaeogeog. Palaeoclim. Palaeoecol.*, **1**, 13 (1965).
- 14 Kawai, N., and Hirooka, K., *J. Geomag. Geoelect.*, **19**, 217 (1967).
- 15 Jacobs, J. A., *Nature*, **230**, 574 (1971).
- 16 Bray, J. R., *Nature*, **228**, 353 (1970).
- 17 Lundqvist, J., *Sver. Geol. Unders. Ser. C*, No. 554 (1957).

LETTERS TO NATURE

PHYSICAL SCIENCES

Evidence for Amino-acids of Extraterrestrial Origin in the Orgueil Meteorite

THE Orgueil meteorite¹, a Type I carbonaceous chondrite that fell in France in 1864, has a high carbon content of about 5 per cent. It has been reported to contain several organic compounds, but some of these compounds, notably amino-acids²⁻⁴, have been suspected of being terrestrial contaminants⁴⁻⁷. Until recently it has been difficult to determine the extent of the contamination which occurred between the time of fall of a meteorite and its examination in the laboratory. Now, however, the problems of separation of contaminant from indigenous amino-acids in meteorites can be largely overcome by applying gas chromatographic techniques for the separation of D,L enantiomers of amino-acids as their diastereomeric derivatives and the identification of these compounds by gas chromatographic retention times and mass spectral fragmentation patterns. This kind of approach has been used in investigations of the amino-acids in the Murchison and Murray meteorites⁸⁻¹¹. Because terrestrial, biogenic amino-acids are commonly of the L configuration, the presence in these meteorites of racemic mixtures of D,L amino-acids suggested a nonbiogenic origin for these compounds. In addition, the presence of amino-acids not commonly found in protein also strongly implied an extraterrestrial, abiotic origin.

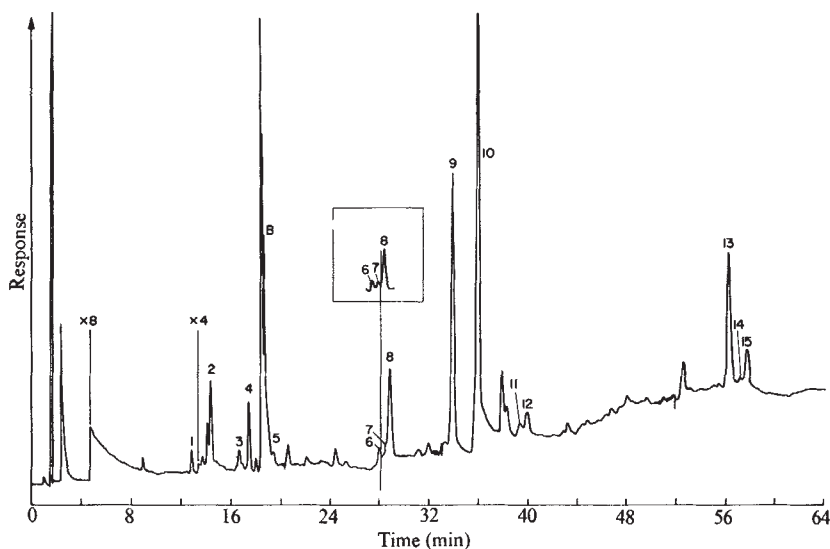
This investigation of the Orgueil meteorite was undertaken to determine which amino-acids can be obtained by the application of techniques used previously on Murchison and Murray meteorites^{8,9,11}. If earlier interpretations were correct, the Orgueil meteorite should contain a dominance of L isomers of the common protein amino-acids which represent terrestrial contamination. Thus, the occurrence of any D isomer might indicate the presence of indigenous amino-acids, while the L isomers might be predominantly the result of con-

tamination. The occurrence of nonprotein amino-acids would be particularly interesting. These would be less common contaminants. The presence of one or more of these amino-acids with asymmetric centres and with nearly equal amounts of both D and L isomers would provide convincing evidence for the indigenous nature of some of the amino-acids that were found.

For this study, two samples of Orgueil meteorite were examined. An account of the experimental procedure has been described elsewhere⁹. The first sample, weighing 7 g, was pulverized in an agate mortar with a pestle, and 4.2 g was refluxed with water for 19 h. This sample was provided by Dr K. Fredriksson of the Smithsonian Institution. It was also used for bulk chemical studies, Mössbauer spectroscopy studies, and for the analysis of other organic compounds. The water extract was recovered and the sample washed with water. The extract and washes were combined and evaporated to dryness. The sample was divided at this point and 1.7 g equivalents were carried through the amino-acid analysis. The rest of the extract was used for other studies. The dried extract was refluxed for 20 h with 6 N HCl, and the resulting hydrolysate was evaporated to dryness, dissolved in water, and chromatographed on a 'Dowex 50' ion exchange column. The column was eluted with water followed by 2 N NH₄OH. The NH₄OH eluate was evaporated to dryness and *N*-trifluoroacetyl-(+)-2-butyl ester derivatives of the amino-acids were prepared. The resulting derivatives were subsequently analysed by gas chromatography and gas chromatography/mass spectrometry. The second sample, weighing 11.1 g, was pulverized in an alumina mortar with a pestle, and 2.1 g was treated in a manner similar to the treatment of the first sample. The two procedural blanks that accompanied these samples did not show the presence of amino-acids.

The gas chromatographic analyses were performed on a Perkin-Elmer 900 gas chromatograph fitted with a flame ionization detector and a UCON 75-H-90,000 wall coated capillary column measuring 46 m by 0.05 cm. The gas chromatograph was temperature programmed from 100° to 150°

Fig. 1 Gas chromatogram of *N*-trifluoroacetyl-(+)-2-butyl esters of amino-acids in acid hydrolysed water extract of sample I of the Orgueil meteorite. The inset shows D-β-aminoisobutyric acid (6) and L-β-aminoisobutyric acid (7) from sample II under slightly different chromatographic conditions. The identifying numbers correspond to those in Table 1. Peak B is the *N*-trifluoroacetyl derivative of ammonia which is also found in the blank.



C at the rate of 1° C/min. The same column and programme conditions were used on a Perkin-Elmer 881 gas chromatograph which was interfaced to a CEC (DuPont) 21-491 mass spectrometer by means of a membrane separator.

Table 1 Amino-acids identified by Mass Spectroscopy and Gas Chromatography

(1) α -Aminoisobutyric acid	(9) Glycine
(2) L-Valine	(10) β -Alanine
(3) D-Alanine	(11) D-Proline
(4) L-Alanine	(12) L-Proline
(5) N-Methylglycine (sarcosine)	(13) γ -Aminobutyric acid
(6) D- β -Aminoisobutyric acid	(14) D-Aspartic acid
(7) L- β -Aminoisobutyric acid	(15) L-Aspartic acid
(8) β -Amino-n-butyric acid	

Detailed examination of the mass spectra and gas chromatographic retention times led to the identification of eleven amino-acids (Table 1). Five of these are commonly found in protein: valine, alanine, glycine, proline, and aspartic acid. The remaining six amino-acids (α -aminoisobutyric acid, N-methylglycine (sarcosine), β -aminoisobutyric acid, β -amino-n-butyric acid, β -alanine, and γ -aminobutyric acid) are not found in protein. It could be argued that β -alanine and γ -aminobutyric acid have arisen from the decarboxylation of aspartic acid and glutamic acid, respectively. But the presence of α -aminoisobutyric acid, β -aminoisobutyric acid, β -amino-n-butyric acid, and sarcosine strongly suggests that the compounds are indigenous. Indeed, the nearly equal concentration of the D and L enantiomers of β -aminoisobutyric acid (Fig. 1) supports the idea that these unusual amino-acids are probably indigenous.

While two gas chromatographic peaks (Fig. 1, peaks 11 and 14) appear to show a higher concentration of D amino-acids (D-proline and D-aspartic acid) than might be expected to result from contamination⁴, these amino-acids fail to meet our criteria for identification which require the co-chromatography of the unknown amino-acid and known standard, and the equivalency of the mass spectrum of the isolated amino-acid with that of an authentic standard. Therefore, while the gas chromatographic retention times for these amino-acids suggested D-proline, and D-aspartic acid, identifiable mass spectra could not be obtained at the low levels of concentrations of these compounds. There are, however, two amino-acids whose D isomers were confirmed by their gas chromatographic retention times and their mass spectra (D- β -aminoisobutyric acid and D-alanine). β -Aminoisobutyric acid is present as a nearly racemic mixture of the D,L isomers and is the only non-protein amino-acid present whose enantiomers are separable by the techniques used. Although the approximately 8% D-alanine may be present as a contaminant from bacterial cell walls⁴, the presence of D-alanine and suggested presence of the D isomers of other common protein amino-acids may indicate that they are indigenous to the meteorite. This possibility is further supported by the presence of other nonprotein amino-acids that would be unusual contaminants. Thus, we conclude that there are amino-acids indigenous to the Orgueil meteorite in addition to those present as contaminants.

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- Baker, B. L., *Space Life Sci.*, **2**, 472 (1971).
- Kaplan, I. R., Degens, E. T., and Reuter, J. H., *Geochim. Cosmochim. Acta*, **27**, 805 (1963).
- Anders, E., DuFresne, E. R., Hayatsu, R., Cavaille, A., DuFresne, A., and Fitch, F. W., *Science*, **146**, 1157 (1964).
- Oro, J., Nakaparksin, S., Lichtenstein, H., and Gil-Av, E., *Nature*, **230**, 107 (1971).
- Oro, J., and Skewes, H. B., *Nature*, **207**, 1042 (1965).
- Vallentyne, J. R., in *Origins of Prebiological Systems* (edit. by Fox, S. W.), 105 (Academic Press, New York, 1965).
- Hamilton, P. B., *Nature*, **205**, 284 (1965).
- Kvenvolden, K., Lawless, J., Perring, K., Peterson, E., Flores, J., Ponnampuruma, C., Kaplan, I. R., and Moore, C., *Nature*, **228**, 923 (1970).
- Kvenvolden, K. A., Lawless, J. G., and Ponnampuruma, C., *Proc. U.S. Nat. Acad. Sci.*, **68**, 486 (1971).
- Oro, J., Gibert, J., Lichtenstein, H., Wikstrom, S., and Flory, D. A., *Nature*, **230**, 105 (1971).
- Lawless, J. G., Kvenvolden, K. A., Peterson, E., and Ponnampuruma, C., *Science*, **173**, 626 (1971).

Aspects of the Distribution of Fossil Species of Calcareous Nannoplankton in North Atlantic and Caribbean Sediments

ALTHOUGH the calcareous nannoplankton have been the subject of considerable research during the past two decades, the factors which influenced the distribution of the fossil representatives of this group have been rather neglected. Several authors, however, allude to features of morphology, for example, thickening within species of *Discoaster*¹⁻⁴ or the distribution of families or species of the calcareous nannoplankton which they attribute to the influence or in some instances lack of influence of ecological factors^{2,3,5}.

In the Recent oceans three factors are known to control the concentration and distribution of nannoplankton species in the

Table 1 The Location, Approximate Absolute Age according to Berggren's Time Scale²⁰, and the Sampled and Inferred Depth of Deposition of the Samples considered in this Report (the latter is indicated by a Dash when no Change in Depth is Inferred)

Sample	Lat.	Long.	Age (m.y.)	Sampled depth (m)	Inferred depth of deposition (m)
G13	40° 14.59' N	75° 58.58' W	48	13	—
G28	40° 14.31' N	73° 59.12' W	48	9	—
JOIDES 6	30° 05' N	79° 15' W	42	805	—
AZ	47° 37.0' N	07° 31' W	48	1,262-1,006	—
D5951	42° 35.8' N	11° 57.5' W	47	1,040-1,013	—
Dog 20	39° 43' N	70° 43' W	48	1,000	—
JOIDES 3	30° 20' N	80° 20' W	49	1,032	—
Gosnold					
49-2150	39° 46' N	69° 44' W	48	1,675	—
A150-1	33° 42' N	62° 30' W	47	1,597	—
C10-1	33° 40' N	62° 30' W	49	1,480	—
A164-25	32° 13' N	64° 31' W	44	1,570	—
A167-21	29° 49' N	76° 35' W	44	1,455	—
D5981.9 *	42° 51.5' N	20° 16.5' W	52	5,282-4,542	1,920
D5968.2 *	42° 50.3' N	20° 12.2' W	49	5,329-4,604	2,140
D5608.4,					
6, 8 *	42° 52' N	20° 16.5' W	49	4,409	2,140
D5608.2 *			48		2,220
D5969.7 *	42° 55' N	20° 11.5' W	48	3,758-3,200	2,220
D5969.2 *			42		2,560
V18-RD37	39° 40' N	65° 55' W	48	2,496-2,166	—
V12-4	24° 16.9' N	53° 04.1' W	48	5,009	1,840
D4799	26° 0.45' N	22° 22.0' W	47	2,356-2,217	—
RC8-2	11° 12' N	48° 05' W	48	4,625	2,320
RC9-55	14° 42' N	70° 53' W	48	3,609	—
RC9-56	14° 38' N	70° 52' W	48	3,404	—
RC9-58	14° 33' N	70° 49' W	48	3,458	—
RC9-59	14° 37' N	70° 50' W	48	3,698	—
V10-96	27° 52' N	54° 38' W	48	4,839	—

* Palmer Ridge samples.

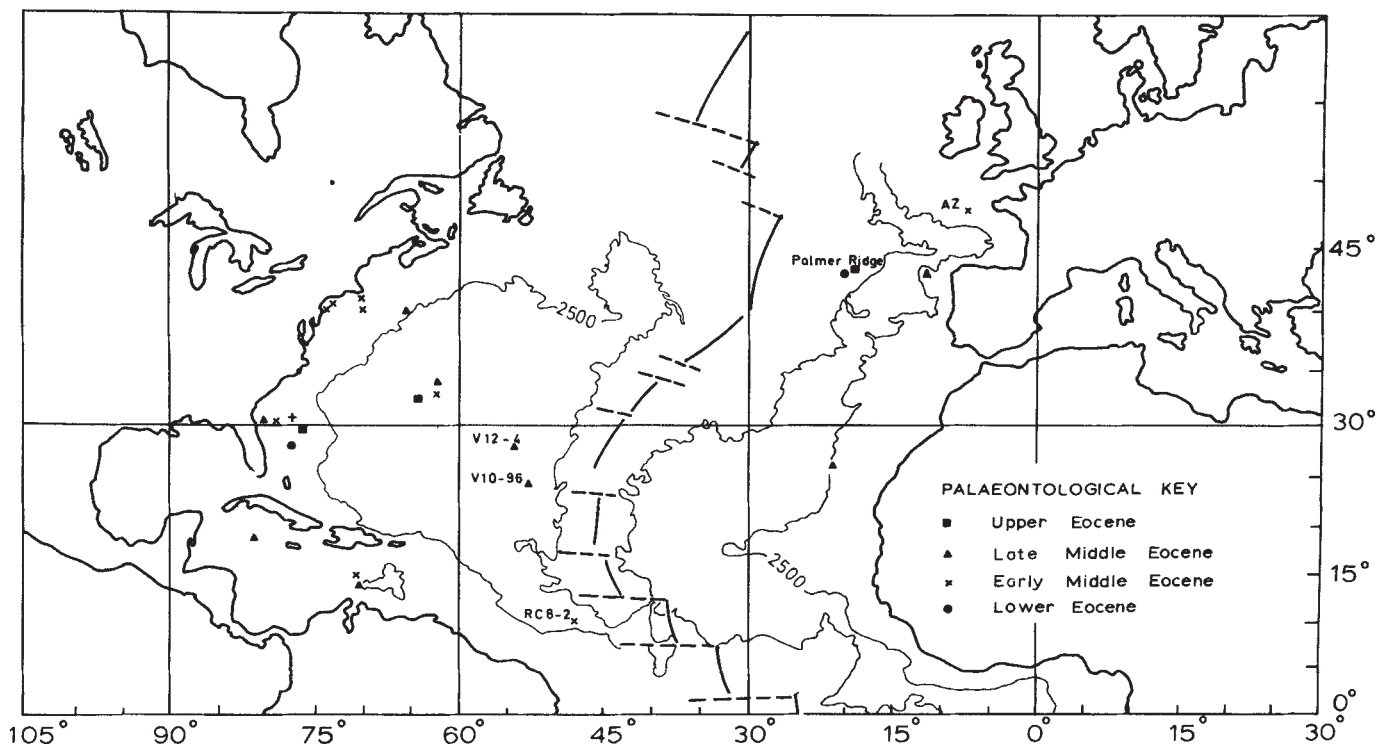


Fig. 1 The North Atlantic with the position of the sampling localities and the crest of the mid-Atlantic Ridge superimposed. Palaeontological ages refer to the oldest fossil occurrence where samples of more than one age were recovered at a locality. The contoured interval is 2,500 fathoms (4,572 m). Localities referred to in the text are indicated.

surface sediments. These are the non-uniform productivity of the surface waters, the environmental preference of individual species and the differential solution of species during and following deposition.

There is no satisfactory method of determining the surface productivity of the past oceans. Although McIntyre and McIntyre⁶ suggest a relationship between coccolith carbonate concentration and surface productivity in recent sediments,

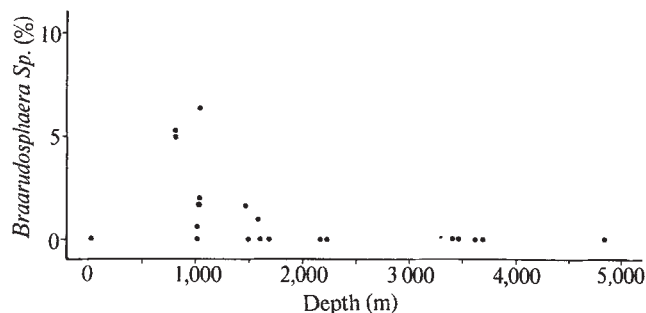


Fig. 3 The relationship between species of *Braarudosphaera* and sampled depth.

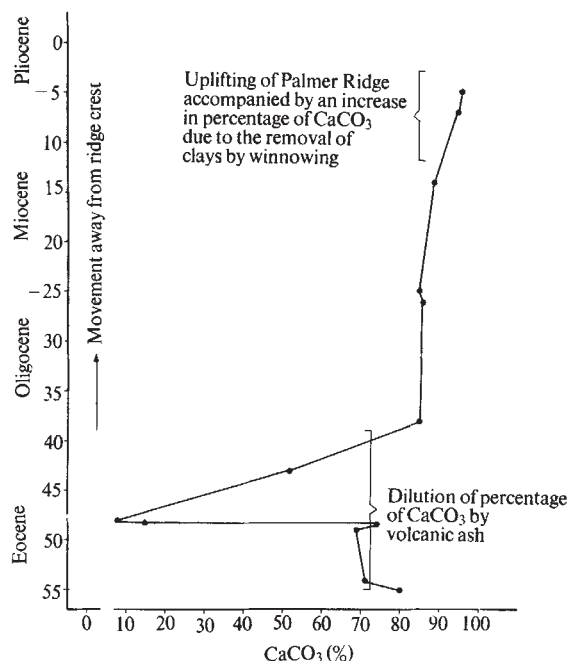


Fig. 2 The relationship between the concentration of CaCO_3 in sediments from Palmer Ridge, and the geological history of this locality; expressed within the framework of a time scale proposed by Berggren²⁰.

CaCO_3 determinations for sediments from two Tertiary localities show that the concentration of this component is influenced by factors other than productivity. At Palmer Ridge (Table 1, Fig. 1) it can be related to the geological history^{7,8} of this locality (Fig. 2), while at locality AZ (Table 1, Fig. 1) the CaCO_3 concentration (ranging from 48% to 84%) is a product of the dilution of calcareous ooze by terrigenous sediments.

The Eocene sediments of the North Atlantic contain no evidence of clearly delineated floral assemblages which can be attributed either to climatic restriction or to the restriction of certain species to particular water masses. In this respect the Eocene North Atlantic differed markedly from its modern counterpart where McIntyre and Be⁹ recognize and equate four distinct nannofloral assemblages with specific surface water isotherms. Species of the related genera *Braarudosphaera*, *Micrantholithus* and *Pemma* are, however, only recorded from sediments deposited around the continental margins and the Bermuda Pedestal. The restriction of these forms to sediments with a sampled depth less than 1,600 m (Fig. 3) is probably the result of environmental preference, which may, as Martini³ has implied, be a function of water salinity and turbidity, or alternatively could have been determined by the depth requirements of a sessile stage in the

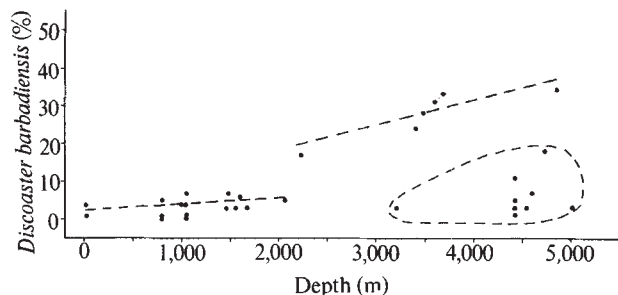


Fig. 4 The relationship between *Discoaster barbadensis* and the sampled depth of all samples from which it is recorded.

pleomorphic life histories of these species. In the modern Atlantic *Braarudosphaera bigelowi* is most abundant in near shore waters.

The relationship between the solution of calcareous tests and depth is already well documented for the planktonic Foraminifera¹⁰⁻¹³ and, to a lesser extent, the calcareous nannoplankton of the modern oceans. It is apparent from the results of these investigations that this phenomenon is selective and favours the preservation of the more robust species in the plankton. In the samples examined here (Table 1, Fig. 1) the proportions of the robust species *Discoaster barbadensis*, *D. ornatus*, and *D. saipanensis* in counts of 300 specimens increase with the sampled depth of the sediment. The relationship between the percentage of *D. barbadensis* and sampled depth is compared in Fig. 4. The discrepant group of samples (circled) were recovered from localities (Palmer Ridge, V12-4 and RC8-2) marginal to the mid-Atlantic Ridge, which have been displaced both horizontally and vertically from their position of deposition by the lateral movement and subsidence of the ocean crust

away from the ridge crest¹⁴. Thus in order to interpret these sediments, or sediments from similarly displaced localities, it is necessary to adjust their positions on the ocean floor for the depth changes which have occurred as a result of seafloor spreading. The adjusted positions of the analysed samples are presented in Figs. 5 and 6. Fig. 5 represents a physiographical reconstruction of the North Atlantic of 40 m.y. ago. In this model it is assumed that the elevation width and slope of the Eocene and Recent mid-Atlantic Ridge are equivalent, and that no appreciable subsidence has occurred around the margins of the Central Atlantic since the Mesozoic. The first assumption is reasoned on the grounds that these parameters, which seem to be related to the spreading rate^{15,16}, would only have differed for the Palaeogene mid-Atlantic Ridge if seafloor spreading had either ceased or increased to 3 cm yr⁻¹ (or above) in the Eocene North Atlantic, neither of which has occurred. The second assumption appears to be supported by the results of Leg 12 of the Deep Sea Drilling Project¹⁷ which suggest that vertical movements occur at the periphery of an ocean during the initial 40-50 m.y. of its formation. In the reconstructed Atlantic Palmer Ridge, V12-4 and RC8-2 lie within the crestal and upper flank provinces of the mid-Atlantic Ridge. Although locality V10-96 shows a similar vertical and lateral displacement its sediments contain a solution induced abyssal nannoflora (60% *Discoaster*), and were probably deposited within a deep linear trough formed by a transform fault. Fig. 6 demonstrates the relationship between the percentage of *Discoaster barbadensis* and the inferred palaeodepth. On this graph the sampled depth and the depth of deposition are considered to be equivalent at all localities other than Palmer Ridge, V12-4 and RC8-2. The depths of deposition of these localities within the Eocene have been derived by calculating their position on the slope of the mid-Atlantic Ridge from the approximate

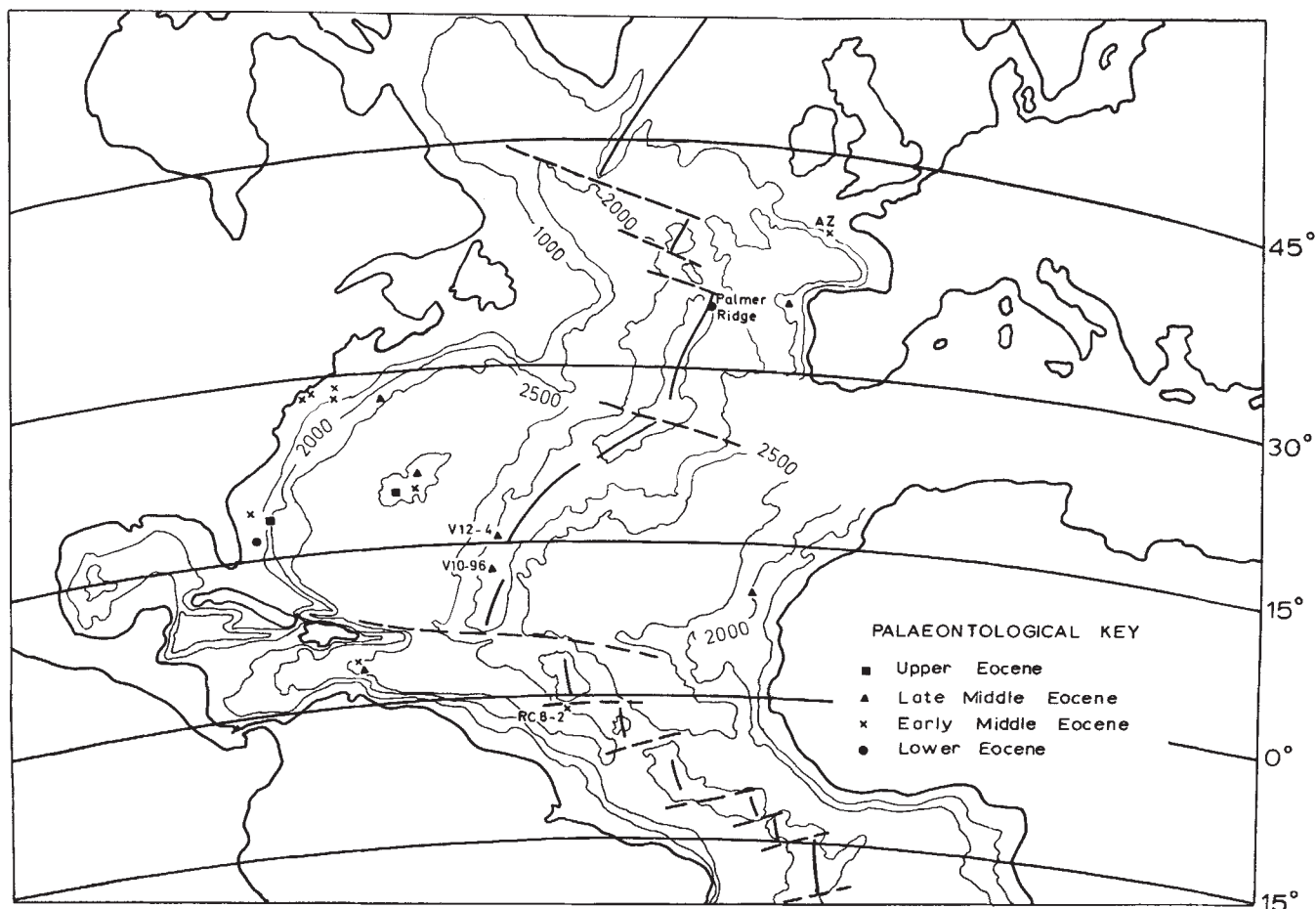


Fig. 5 Reconstruction of the North Atlantic basin of 40 m.y. ago, after Francheteau²¹, with the positions of the sampled localities, the crest of the mid-ocean ridge, and the inferred palaeobathymetry superimposed. The intervals contoured are the 1,000 fathoms (1,828 m), 1,500 fathoms (2,743 m), 2,000 fathoms (3,657 m) and 2,500 fathoms (4,572 m). Localities referred to in the text are indicated.

absolute age of the sediments (Table 1) and the following spreading rates; Palmer Ridge 1.2 cm yr^{-1} (calculated from the age of the basement^{7,8} at this locality), V12-4 1.5 cm yr^{-1} (ref. 18) and RC8-2 1 cm yr^{-1} (ref. 19).

The increase in the proportion of *D. barbadiensis* in sediments deposited at a depth greater than 2,200 m (Figs. 4 and 6) probably reflects a level of increased CaCO_3 solution in the Eocene North Atlantic, below which the more delicate species in the nannoflora were selectively removed at the sediment water interface.

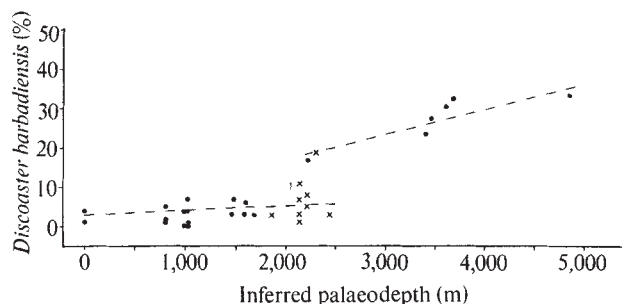


Fig. 6 The relationship between *Discoaster barbadiensis* and inferred depth of deposition. Samples denoted by an X refer to localities which have been adjusted for the depth changes which occurred during seafloor spreading.

It is apparent from the results outlined above that environmentally or chemically induced variations in the species composition of fossil nannoplankton assemblages provide information on the depth and environment of deposition. Apart from providing a means of recognizing sediments which are displaced either by slumping or by vertical movements of the ocean crust since the Eocene, such information is useful for comparing sediments in the oceans with those found on land.

This research was supported by an NERC grant. I thank the Lamont-Doherty Observatory, the US Geological Survey and the University of Miami for providing samples, and Dr Jean Francheteau for permission to reproduce his reconstruction of the Eocene North Atlantic. The calcium carbonate analyses are by Mr R. Burns, and the diagrams by Mrs June Irvine.

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- ¹ Bramlette, M. N., and Riedel, W. R., *J. Paleontol.*, **28**, 385 (1954).
- ² Bramlette, M. N., and Sullivan, F. R., *Micropaleontology*, **7**, 129 (1961).
- ³ Martini, E., in *Submarine Geology and Geophysics*, 393 (Butterworth, London, 1965).
- ⁴ Ramsay, A. T. S., in *Scanning Electron Microscopy: Systematic and Evolutionary Applications*, 179 (Academic Press, New York, 1971).
- ⁵ Worsley, T., and Martini, E., *Nature*, **225**, 1242 (1970).
- ⁶ McIntyre, A., and McIntyre, R., in *The Micropalaeontology of Oceans* (Cambridge University Press, in the press).
- ⁷ Cann, J. R., and Funnell, B. M., *Nature*, **213**, 661 (1967).
- ⁸ Ramsay, A. T. S., *Marine Geol.*, **9**, 261 (1970).
- ⁹ McIntyre, A., and Be, A. W. H., *Deep Sea Res.*, **561** (1967).
- ¹⁰ Berger, W. H., *Science*, **156**, 383 (1967).
- ¹¹ Berger, W. H., *Deep Sea Res.*, **15**, 31 (1968).
- ¹² Berger, W. H., *Marine Geol.*, **8**, 111 (1970).
- ¹³ Berger, W. H., and Parker, F. L., *Science*, **168**, 1345 (1970).
- ¹⁴ Menard, H. W., *Earth Planetary Sci. Lett.*, **6**, 275 (1969).
- ¹⁵ Vogt, P. R., and Ostenso, N. A., *Nature*, **215**, 810 (1967).
- ¹⁶ Menard, H. W., *Science*, **157**, 923 (1967).
- ¹⁷ Laughton, A. S., et al., *Summary of Deep Sea Drilling Project Leg XII* (1970).
- ¹⁸ Talwani, M., Pitman, W., and Heirtzler, J. R., *Trans. Amer. Geophys. Union*, **50**, 189 (1969).
- ¹⁹ Funnell, B. M., and Smith, A. G., *Nature*, **219**, 1238 (1968).
- ²⁰ Berggren, W. A., *Nature*, **224**, 1072 (1970).
- ²¹ Francheteau, J., thesis, Univ. California (1970).

Significance of Weathering in a Pennsylvanian Sandstone to Pollution from Strip Mines

WE discuss here some of the factors relevant to the formation of acid in the spoil heaps that result from surface mining of the Upper Freeport coal in northern West Virginia. The coal is overlaid by the Lower Mahoning sandstone¹, a uniform, quartzose, channel-fill sandstone that can be 30 to 50 feet thick. Pyrite (FeS_2) is the chief acid-forming species in the sandstone².

Pulverized samples of the sandstone ($< 250 \mu\text{m}$) were analysed for total sulphur using a LECO induction furnace and automatic sulphur titrator. KIO_3 titrant concentrations of $1.29 \times 10^{-4} \text{ M}$ and $5.18 \times 10^{-3} \text{ M}$ were used to cover the range of sulphur concentrations. The determinations of exchangeable calcium, magnesium, potassium and aluminium, and of available plant nutrient elements, followed standard methods³.

Sulphate only occurs in traces in the rock, so total sulphur content can be used as a measure of the acid-forming potential in cases where the sandstone is the only rock between the coal and the soil, except in the top 1 m where the sulphur is chiefly organic. Fig. 1a is a diagrammatic summary of these data.

Pyritic sulphur content seems to be related to the colour of the sandstone. In the upper part of the stratum, which contains less sulphur than the lower part, chromas of pulverized samples are greater than 2 (brown, *Munsell Soil Color Charts*⁴), whereas in the lower part, which has a higher sulphur content, the chromas are less than 2 (grey). Black or grey strata near the coal seam consistently contain more than 0.1% sulphur, and chromas are zero.

Petrographic examination of thin sections shows that pyrite is scarce or absent in the top 6 m of Lower Mahoning sandstone, but is common at greater depths. In the top 6 m segregated hydroxides of iron constituting the higher chroma are prominent, enclosing in some cases small residues of pyrite crystals. The strata of lower chroma all contain easily recognizable euhedral pyrite, replacing quartz or mica along grain boundaries or hairline cracks.

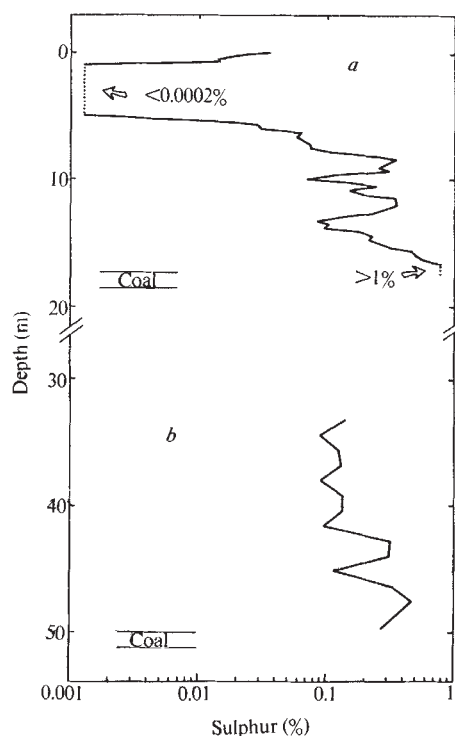


Fig. 1 Typical sulphur concentration in Lower Mahoning sandstone occurring at various depths, (a) near surface, analyses of rotary drill chips; (b) deeply buried, analyses of sections of solid 5 cm diameter test core.

Where the sandstone has remained buried and natural weathering has not yet reached into it, the sulphur content decreases from several tenths of a per cent near the coal to less than one tenth of a per cent near the top of the sandstone. There is no region similar to the highly leached weathered zone observed in the same sandstone when it contacts the surface. The pattern is shown in Fig. 1b.

A few of the rock columns sampled to 16 m show no high-sulphur zone and have chromas higher than 2. Mild geological folding at these locations has resulted in rock fracture with subsequent weathering reaching greater depths. In such cases, a study of the fresh high walls resulting from mining operations verifies suspected lateral penetration of weathering from fractures, indicated by iron oxide chromas enclosing an interior of massive, low-chroma sandstone at depths below the 6 m weathered zone indicated in Fig. 1. This lateral penetration of weathering, extending inward several centimetres from the vertical fissures, vividly illustrates the "weathering front" (ref. 6). Evaluation of chromas in such bicoloured specimens consistently distinguishes between high sulphur and low sulphur portions of the fragments (Table 1).

Table 1 Sulphur in Relation to Chroma in Six Natural Bicoloured Fragments of Lower Mahoning Sandstone*

Fragment	Chroma	Position in fragment	Sulphur (%)
1	4	Near surface	<0.001
1	0	Interior	0.175
2	3	Near surface	0.048
2	0	Interior	0.288
3	6	Near surface	0.060
3	0	Interior	0.198
4	6	Near surface	<0.001
4	0	Interior	0.035
5	4	Near surface	0.032
5	0	Interior	0.140
6	6	Near surface	0.004
6	2	Interior	0.010

* Ground to <250 μ m; colour evaluated on dry sample.

Higher chromas penetrate several centimetres from bedding or fracture planes, low chromas typify interiors.

Although the presence of sulphides, other reduced chemical species, and low chroma (grey) coloration might indicate the effects of the water table, the 6 m depth from the present land surface is well above the present permanent water table. The evidence for oxidation to greater depths on fracture planes confirms that a permanent water table is not involved. Prolonged saturation of the sandstone is a likely condition within the rock that has retained its low chroma colour and pyrite. This condition is related to rock porosity, position in the section, recharge by meteoric water, and rock chemistry. Details of these influences have not been studied, but their resultant interactions evidently have maintained an oxidation potential low enough to preserve pyrite in the low chroma rock.

The inherent low fertility of soil developed from Lower Mahoning sandstone¹ is readily understood in view of the properties of the pre-weathered parent material. The solubilization and subsequent leaching of all but the most acid-insoluble compounds by the sulphuric acid formed by oxidation of the pyrite in the weathering sandstone have left rock which is almost barren of plant nutrients. Measurements of available plant nutrient cations throughout the depths studied indicate intense removal of essential plant nutrients from the 6 m oxidized zone. This strong acid leaching during the early stages of soil development accounts for low base saturation levels and modern classification of these soils as Dystrochrepts or Udults⁷.

The usual method of spoil disposal in this area is backfilling and covering with material favourable for planned land use, usually afforestation, forage growth, or specialty uses. The total sulphur and chroma profiles in near-surface Lower Mahoning sandstone indicate that there are adequate volumes

of pyrite-free rock material to place in the oxidation zone of spoil heaps to avoid acid pollution. But nutrients must be added before vigorous vegetation can be established. On the other hand, the bulk of potentially toxic low chroma material below a depth of 6 m constitutes a formidable barrier to revegetation and a likely prolonged source of acid water pollution unless protected from oxidation by burial or other means. Studies are under way to determine weathering of spoil materials, rate of plant nutrient release, and the progress of soil property genesis, which are expected to proceed differently in fractured spoil materials than in stratified sediments *in situ*.

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- White, I. C., *Bull. US Geol. Surv.*, No. 65 (1891).
- Grimsley, G. P., *Iron Ores, Salt and Sandstones*, West Virginia Geol. Surv., 4 (1909).
- Jackson, M. L., *Soil Chemical Analysis* (Prentice-Hall, 1958).
- Munsell Soil Color Charts* (Munsell Color Co., Inc., Baltimore, Maryland).
- Temple, K. L., and Koehler, W. A., *Drainage from Bituminous Coal Mines*, West Virginia Eng. Exp. Sta. Res. Bull. No. 25 (1954).
- Ollier, C., in *Weathering* (American Elsevier, New York, 1969).
- Soil Survey Staff, *Placement of Series—Northeast Region*, USDA-SCS (Northeast Regional Technical Service Center, Upper Darby, Pennsylvania, 1969).

BIOLOGICAL SCIENCES

Defective Synthesis of α and β Globin Chains in Lead Poisoning

THE cells of many tissues, including bone, red cells, liver, brain and nerves, absorb lead¹ which accumulates chiefly on the mitochondrial membrane. Here it disturbs mitochondrial metabolism and produces the swelling and disruption revealed by electron microscopy². The most obvious metabolic defect is the inhibition of the synthesis of haem (and porphyrin). Lead inactivates at least three mitochondrial enzymes in the haem pathway (δ aminolaevulinic acid synthetase³, δ -aminolaevulinic dehydratase³, and haem synthetase⁴). This aspect of lead toxicity (reviewed in ref. 5) reduces haem production and leads to the accumulation and excessive excretion of several porphyrin intermediates. Lead seems to affect red cells chiefly by causing increased destruction and interfering with haemoglobin synthesis, as judged by the presence of ring sideroblasts in the bone marrow and hypochromia of the red cells. In normal red cell precursors the synthesis of haem and globin is finely balanced, but in diseases such as sideroblastic anaemia⁷ and iron deficiency anaemia (R. Barr, A. V. Hoffbrand and J. M. W., unpublished) a defect in haem synthesis leads to a disturbance of globin synthesis. A previous report indicated that globin synthesis was defective in lead poisoning⁸, but no reports have dealt with the synthesis and assembly of α and β chains, which we have now studied.

Reticulocyte-rich blood samples from 3 yr old twins, who had developed lead poisoning after eating old paint, were prepared and incubated for 60 min with ³H-leucine and the cells were divided into two equal aliquots. From one aliquot we prepared "impure" globin by adding the cells directly to

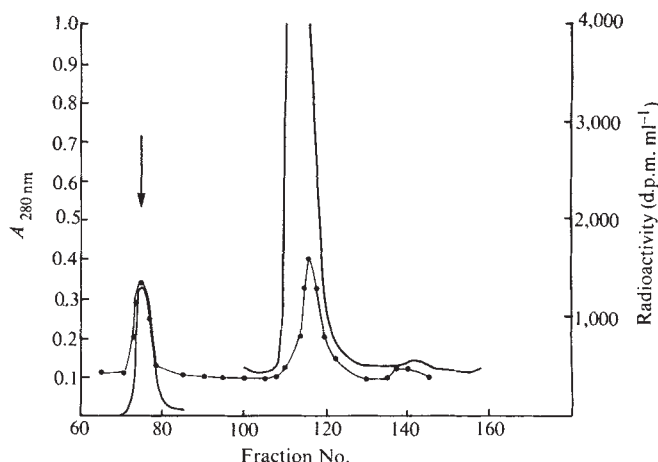


Fig. 1 Pattern of radioactivity of protein fractions of lysate of twin 1 separated by 'G-100 Sephadex' chromatography. —, Absorbance 280 nm; ●—●, radioactivity (d.p.m. ml⁻¹). Note that the radioactivity associated with the dextran blue peak (arrow) is nearly as great as that associated with haemoglobin peak.

acid acetone. From the other aliquot we made "pure" globin by separating the haemoglobin from other proteins by chromatography of a lysate of washed cells on 'G-100 Sephadex'. The radioactivity and absorbance of the protein fractions of the lysate eluted from the column were measured. Finally, the pure haemoglobin fraction was concentrated by ultrafiltration and the globin precipitated by addition of acid acetone. The α and β chains from impure and pure globins were separated by chromatography on CMC-23 using 8 M urea-phosphate buffers⁹. The radioactivity associated with the α and β chain protein peaks was measured, and then the total radioactivity of each peak was determined (Table 1). The synthesis of α and β chains of their reticulocytes was measured *in vitro*, at the time the patients first presented and 6 and 12 weeks later while they were recovering after treatment with penicillamine.

When first studied the patients' haemoglobin levels were 7.0 and 7.6 g 100 ml.⁻¹ and blood lead levels 98 μ g 100 ml.⁻¹. The radioactivity of the protein fractions of the cells separated by chromatography on a 'G-100 Sephadex' is shown in Fig. 1. (Only the results of one twin are shown: the other twin's results are identical.) Two important features are shown. First, the radioactivity of the void column peak is nearly as great as the radioactivity of the pure haemoglobin fraction. (This peak contains ribosomes and apoferritin and its radioactivity is normally only one-twentieth to one-fifteenth of the radioactivity associated with the haemoglobin fraction.)

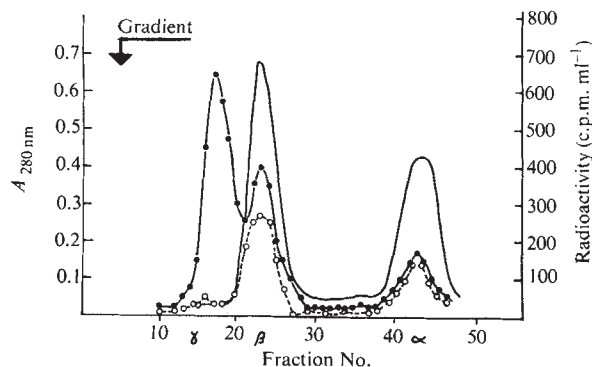


Fig. 2 First experiment. Pattern of radioactivity as associated with the α and β chains of twin 1, separated on CMC-23. —, Absorbance 280 nm; ●—●, "impure" globin (c.p.m. ml⁻¹); ○—○, "pure" globin (c.p.m. ml⁻¹). Note: (1) in "impure" globin large amount of " γ " peak radioactivity; β chain radioactivity > α chain radioactivity; (2) in "pure" globin " γ " peak has disappeared; fall in β chain radioactivity but all α chain radioactivity recovered.

Table 1 Laboratory Investigations on Patients

	Twin 1	Twin 2
Hb (g 100 ml. ⁻¹)	7.3	7.6
MCHC (%)	28.0	27.5
Reticulocytes (%)	10.0	11.5
Blood lead (μ g 100 ml. ⁻¹)	98.0	98.0
Ub F (%)	3.2	3.0
Hb A ₂ (%)	1.3	1.8
Hb electrophoresis	A	A

Second, the amount of radioactivity associated with haemoglobin fraction (3,000 d.p.m. ml.⁻¹) is very low for a reticulocyte count of 10%. Together these findings indicate indirectly that the synthesis of the haemoglobin tetramer is abnormal. Direct evidence for this was obtained from studies of the synthesis of the isolated α and β chains.

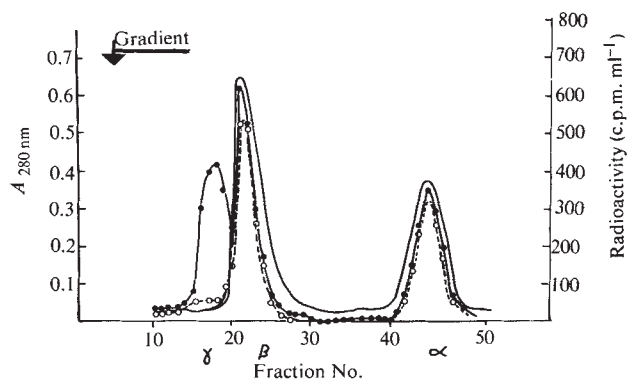


Fig. 3 Second experiment. Pattern of radioactivity of α and β chains of twin 1. Note: (1) in "impure" globin fall of " γ " peak activity and relative increase in β chain and α chain radioactivity; (2) most of the β and α chain radioactivity recovered from "pure" globin.

The radioactivity associated with the α and β chains isolated from the impure globin preparations is shown in Fig. 2. Most of the radioactivity was found in a peak in front of the β chain peak in the region corresponding to the γ chain. This peak is called " γ ". The radioactivity of the β chain was less than this initial peak but significantly greater than that associated with the α chain peak. The ratios of the radioactivity of the α : β + " γ " chains were 0.23 and 0.25 in twin 1 and twin 2, respectively, and the ratios of the radioactivity of the α : β chains alone, 0.60 and 0.61. The pattern of radioactivity associated with the α and β chains isolated from pure globin preparations showed several differences. The " γ " peak of radioactivity had disappeared and there was a fall in the radioactivity of the β chains. Virtually all the radioactivity associated with the α chain in the impure globin sample, however, was recovered in the α chain isolated from the pure globin. Six weeks later the pattern of radioactivity obtained after elution of the impure globin preparation shows a fall in radioactivity associated with the " γ " peak and a relative increase in the radioactivity associated with the β and α chains (Fig. 3). The pattern of radioactivity of the chains isolated from the pure globin preparation was very similar except that the " γ " peak was missing and the specific activity of the β chain was reduced. The ratios of radioactivity of α : β + " γ " peaks made from the impure globin were 0.65 and 0.68 and the α : β ratios 0.83 and 0.87. The findings of the final experiments, 12 weeks later, are shown in Fig. 4. The radioactivity of the " γ " peak had disappeared and the radioactivity of the α and β chain peaks from both the pure and impure globin preparations was very similar. The ratio of the radioactivity of α : β + " γ " chains was 0.89 and 0.90 and the α : β ratio 0.93 and 0.96. Fig. 5 shows the ratios of radioactivity of the α : β + " γ " chains made from impure globin preparations from each twin

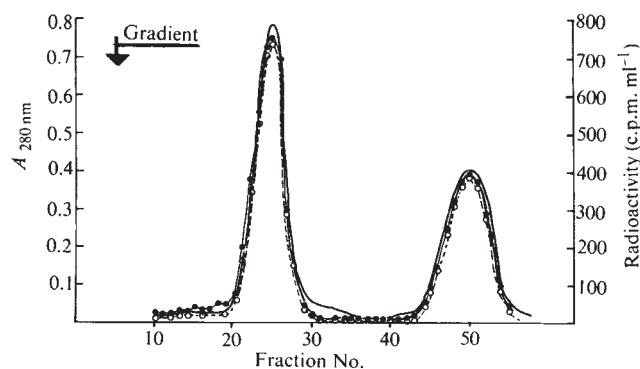


Fig. 4 Third experiment. Pattern of radioactivity of α and β chains, twin 1. Note: absence of " γ " radioactivity and nearly equal amounts of β and α chain activity, most of which is recovered from the "pure" globin.

plotted against the haemoglobin values. As the haemoglobin levels rise, and the blood lead levels fall, the $\alpha : \beta + \gamma$ ratio becomes near to 1.0.

These findings indicate that in the reticulocytes of the patients globin synthesis is disordered. In the initial experiments, the β chain peak of the impure globin preparation was more radioactive than the α chain peak. Because the chains were isolated from whole cells this finding indicates that the total synthesis of β chains was greater than that of α chains. But radioactivity of the α chain peak was virtually the same in the impure and pure globin preparations, which indicates that nearly all the α chains synthesized combine with β chains and haem to form haemoglobin. The finding that the radioactivity of the β chain peak was less in the pure globin preparations again suggests that there was a relative excess of β chains which existed as a free (uncombined) pool.

The nature of the " γ " peak is uncertain. A similar peak of activity has been found in preparations made from marrow cells cultured without haem^{10,11}. The peak was originally thought to be due to the synthesis of true γ chains¹⁰, but recent analysis has shown it to be a protein of a larger molecular weight with a different peptide sequence¹¹. An alternative suggestion is that it is apoferritin¹¹. Our data support this as we were unable to demonstrate this peak in the pure preparations and also found a large amount of radioactivity associated with the apoferritin peak after 'G-100 Sephadex' chromatography. Moreover, the level of Hb F ($\alpha_2\beta_2$) in the two patients was never greater than 3% and higher levels would have been expected if this peak was true of γ chain.

A similar although lesser degree of defective synthesis is seen in two other conditions due to haem deficiency, namely sideroblastic anaemia⁷ and iron deficiency anaemia (R. Barr, A. V. Hoffbrand and J. M. W., unpublished). It is tempting

to postulate that lead, in addition to its undoubted effect on haem synthesis, directly affects the synthesis and/or assembly of the globin chains. In support of this conclusion, when reticulocytes are incubated with lead *in vitro* polysomal disaggregation occurs¹². This has also been observed in reticulocytes with haem (iron) deficiency, however, and the disordered synthesis in lead poisoning may be wholly due to haem deficiency.

It is uncertain whether protein synthesis is disturbed in other cells but in reticulocytes the abnormal synthesis of globin chains seems to be a factor in the pathogenesis of the anaemia of lead poisoning.

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- Barry, P. S. I., and Mossman, D. B., *Brit. J. Indust. Med.*, **27**, 339 (1970).
- Bessis, M., and Breton-Gorius, J., *Blood*, **19**, 635 (1962).
- Dresel, E. I. B., and Falk, J. E., *Biochem. J.*, **63**, 80 (1965).
- Goldberg, A., Ashenbracker, H., Cartwright, G. E., and Wintrobe, M. M., *Blood*, **11**, 821 (1956).
- Goldberg, A., *Seminars Haematol.*, **5**, 424 (1968).
- Waldron, H. A., *Brit. H. Indust. Med.*, **23**, 83 (1964).
- White, J. M., Brain, M. C., and Ali, M. A. M., *Brit. J. Haematol.*, **20**, 263 (1971).
- Kasenaar, A., Morell, H., and London, I. M., *J. Biol. Chem.*, **229**, 423 (1957).
- Clegg, J. B., Naughton, M. A., and Weatherall, D. J., *J. Mol. Biol.*, **19**, 91 (1966).
- Gabuzda, T. G., Melvin, M., Silver, R. K., and Sachs, C., *Proc. Thirteenth Congr. Intern. Soc. Haematol.*, **8** (1970).
- Wood, N., Whittaker, J. A., Clegg, J. B., and Weatherall, D. J., *Abst. Brit. Soc. Haematol.*, **19** (1971).
- Trakatellis, A. C., Heinle, E., Montjar, M., Axelrod, A. E., and Jensen, W. N., *Arch. Biochem. Biophys.*, **112**, 89 (1965).

Transmission of Scrapie to the Cynomolgus Monkey (*Macaca fascicularis*)

SCRAPIE has been transmitted to the cynomolgus, or crab-eating, monkey (*Macaca fascicularis*) with an incubation period of more than 5 yr from the time of intracerebral inoculation of scrapie-infected mouse brain. The animal developed a chronic central nervous system degeneration, with ataxia, tremor and myoclonus with associated severe scrapie-like pathology of intensive astroglial hypertrophy and proliferation, neuronal vacuolation and status spongiosus of grey matter. The strain of scrapie virus used was the eighth passage in Swiss mice (NIH) of a Compton strain of scrapie obtained as ninth intracerebral passage of the agent in goat brain, from Dr R. L. Chandler (ARC, Compton, Berkshire).

The monkey, a juvenile cynomolgus, was inoculated on April 18, 1966, with a 10% suspension of the scrapie-infected mouse brain in phosphate buffered physiological saline, pH 7.4, which had been clarified by centrifugation at 3,500 r.p.m. for 30 min. The animal received 0.2 ml. of such suspension by each of five routes: intracerebral, intravenous, intraperitoneal, intramuscular and subcutaneous. This suspension had an LD₅₀ infectivity titre of 10^{-7.5} ml.⁻¹ by intracerebral inoculation in mice.

Five years and five months after inoculation, the animal developed slight ataxia and tremors of the head and extremities. These signs became progressively more severe with generalized body tremors more prominent during feeding and on agitation. By 6 weeks after onset there was pronounced locomotor ataxia and clumsiness in handling food and myoclonic jerks were

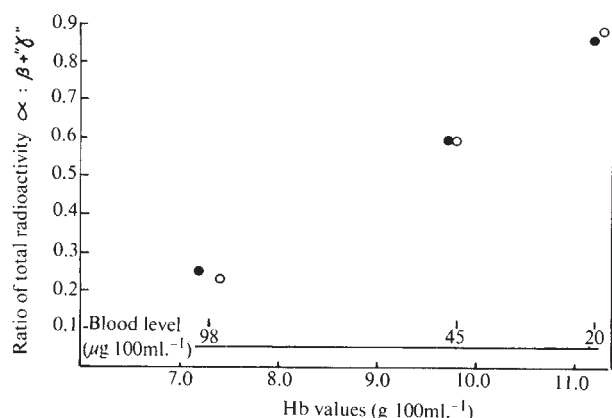


Fig. 5 Correlation between ratios of total radioactivity of the $\alpha : \beta + \gamma$ chains with haemoglobin values of both twins. Blood lead levels are also indicated. ●, Twin 1; ○, twin 2.

noted. The animal became hyperexcitable with exaggerated startle response; it remained alert and active during 2 months of illness, with progressively advancing motor debility. Appetite remained good; no paresis or paralysis developed and there were no signs of illness in systems other than the central nervous system. No convulsions, fasciculations, somnolence or coma developed, and no eye signs were noted.

The animal was killed in advanced disease 2.5 months after onset. At necropsy no gross abnormalities were found. Brain and other visceral tissues were taken for pathological and virological studies.

Shortly before death, the cerebrospinal fluid was clear, colourless, with 0–1 mononuclear cells mm⁻³; 2 months after onset haematological studies and numerous blood chemistry determinations were within normal limits.

Preliminary pathological study of the brain by Drs Kenneth Earle, Reid Heffner (Armed Forces Institute of Pathology, Washington, DC) and Peter Lampert (Department of Pathology, University of California School of Medicine, La Jolla) revealed extensive neuronal vacuolation and advanced status spongiosis in cerebral cortical and cerebellar areas. There was a moderate glial proliferation, but no leucocytic infiltration was noted. A more detailed neuropathological report is in preparation.

Brain suspension from this animal has been inoculated into monkeys of several species, including additional cynomolgus monkeys, and into mice, rats, hamsters and gerbils.

In addition to the cynomolgus monkey, one chimpanzee, one rhesus and one African green monkey were similarly inoculated with brain suspension of the same eighth mouse passage scrapie virus. These three animals remain well 68 months after inoculation. This strain of scrapie virus in fourth mouse brain passage was inoculated 7 yr 4 months ago into four rhesus monkeys; these animals remain well. The ninth mouse brain passage of this virus was inoculated into one squirrel monkey 18 months ago, and two squirrel monkeys and one spider monkey 9 months ago. These still healthy animals remain under observation.

The original ninth passage goat brain received from Dr R. L. Chandler was inoculated intracerebrally 4 yr ago into one chimpanzee, one rhesus and one cynomolgus monkey; and 9 months ago into two squirrel monkeys. These five animals remain well.

An American strain of scrapie virus from a sheep which was killed in advanced disease, in Illinois, was inoculated as a 10% sheep brain suspension by all five routes into one chimpanzee, one rhesus and one cynomolgus monkey 4 yr ago. Brain from a second American scrapied sheep was inoculated 9 months ago into two squirrel monkeys, and at that time two squirrel monkeys and one spider monkey received intracerebral injections of the third mouse brain passage of the Illinois strain of American scrapie. These eight animals remain well.

Because of the long incubation period, we are reporting this first transmission of scrapie to a single primate, before further primary or passage transmissions have occurred.

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Suppression of the Immune Response: Reversal of the Disease State with Antigen in Allergic Encephalomyelitis

EXPERIMENTAL allergic encephalomyelitis (EAE) is an autoimmune disease which is characterized^{1,2} primarily by lymphocytic inflammation and demyelination of the white matter of the central nervous system (CNS); clinical signs generally

include lower limb paralysis, ataxia, tremors and death^{3,4}. Of numerous factors proposed for EAE induction, it is now established that the A1 protein, the basic protein of CNS myelin (molecular weight 18,400), which comprises 30% of the myelin protein¹, is the encephalitogenic agent of CNS tissue^{1,5,6}. The complete amino-acid sequence of the bovine⁷ and human^{7,8} A1 proteins has now been determined, thus making possible the correlation between chemical structure and immunological properties. The suggested open double-chain conformation⁹ of this protein, in contrast to a globular structure, emphasizes the primary structure in defining its antigenic properties, and has simplified the identification of the disease-inducing sites as they can be obtained as isolated peptide fragments. One peptide of forty-five amino-acids, residues 44–89 of the A1 sequence^{10,11}, induces EAE in the rabbit. A major encephalitogenic determinant¹² in both guinea-pigs and rabbits contains only nine amino-acids (residues 114–122) (refs. 13, 14) including the single tryptophan residue. Phylogenetic variation is emphasized by the finding¹⁵ of another region, residues 134–170, which defines the major encephalitogenic determinant for the rhesus monkey.

The manipulation of the immune response to achieve a state of immunological paralysis¹⁶ is an important therapeutic objective in human disease, particularly in autoimmune disease, tissue transplantation, and cancer. The importance of a well defined antigen in such studies is obvious. Immunological studies on EAE^{17,18} have often been carried out with whole CNS tissue, making interpretation ambiguous. The purified A1 protein, however, has proved highly effective in blocking EAE in guinea-pigs if given before sensitization, and in suppressing EAE if given soon after^{19–21}. We have confirmed²² this result with the human A1 protein and the 2-hydroxy-5-nitrobenzyl bromide (HNB) derivative using guinea-pigs. Our objective was to investigate the effect of antigen on the most critical state—that is, after unmistakable clinical signs were observed. We used the human A1 protein for EAE induction and suppression in the monkey, rather than the guinea-pig, rat or rabbit which are commonly used, because of the close relationship between EAE in monkeys and post-rabies encephalomyelitis in man^{3,4}. We found in another study¹⁵ that the A1 protein or the HNB derivative induces a reproducible, striking course of clinical and histological manifestations of EAE in the monkey virtually identical to that induced by whole CNS tissue as described by Kabat *et al.*²³.

We used rhesus monkeys (young adults, 2–4.5 kg) which were free of tuberculosis, diarrhoea and infection and were given medical examinations periodically for *Shigella sonnei*, *Salmonella*, and tubercle bacilli. The diet consisted of Purina monkey chow and fresh fruit. EAE was induced by intradermal injections in both foot pads of a total of 5 mg of a homogeneous preparation of human A1 protein²⁴ homogenized with Difco complete Freund's adjuvant containing 0.1 mg of *M. tuberculosis* (H37Ra). Sensitized animals were observed daily for clinical signs^{1,15,23} such as anorexia, which always preceded the other signs by 1–5 days, ptosis of eyelids, tremors, lethargy, ataxia, loss of coordination, leg weakness or paralysis. These signs developed 13–26 days after sensitization and increased in severity until the animal died.

Suppressive treatment was initiated by intramuscular injection of human protein (usually 10 mg) emulsified in Difco incomplete Freund's adjuvant (40 mg A1 protein/ml. saline combined with an equal volume of incomplete adjuvant). When the A1 protein was in saline solution, complexed with alum, or pretreated with glutaraldehyde, it seemed less effective. HNB-modified A1 protein with blocked tryptophan residue^{25,26} was also used for suppressive treatment. Therapeutic injections were usually given within 24–48 h after unmistakable signs of EAE. After the first injection, 2–3 mg of antigen was given daily similarly for at least 12 days. A total of 36–65 mg of A1 protein or HNB derivative was usually required. Control animals were either not injected or were given the same treatment using calf thymus histone instead of A1 protein.

Table 1 Suppression of EAE in Rhesus Monkeys after Appearance of Clinical Signs

Suppressive * treatment	Total No. of animals	No. developing clinical signs	No. dead	No. recovered
A1 protein	12	12	3	9
HNB-A1 protein	4	4	0	4
Histone	10	10	10	0
None	10	10	10	0

* EAE was induced in all monkeys by injection into the footpad of a total of 5 mg A1 protein (human) in complete Freund's adjuvant. Suppressive treatment, with the material indicated, was begun when unmistakable clinical signs of ataxia, weakness or paralysis, and loss of coordination had appeared. Anorexia generally preceded these signs by 2-4 days. Control animals died in 1-4 days after general clinical signs were first observed.

In all cases, the animals were given procaine penicillin G (75,000 U/day), and when not eating were force fed twice daily with A-B-dextrose solution (40 ml. total), Allstate Veterinary Supply Company.

The results (Table 1) showed that only three of the sixteen animals treated with either the A1 protein or HNB-A1 protein died, whereas all control animals died. Of the three monkeys, two survived 10 and 23 days where the controls lived for 1-4 days; the third monkey died 20 h after the first injection. Of the surviving animals suppressed with A1 protein, eight were examined for humoral antibody by using a passive haemagglutination assay¹. Three animals had antibody titres of 1/64-1/512 at 1-2 weeks after the last injection for suppression.

The histories of four monkeys, successfully suppressed for EAE, are recorded in Table 2; the other survivors, including the HNB derivative-injected group, had a history similar to monkeys I and II. Eight of the surviving animals showed significant improvement in the clinical condition within 24 h after the first injection of A1 protein. This observation was based on several criteria; recovery of appetite (usually a craving for fruit); improved coordination; increased movement and strength; partial return to normal mannerisms; and less ataxia. The condition of the other monkeys either remained the same or became slightly worse on the first or second day after the initial injection, and in three cases the animals remained prostrate on the floor of the cage for 28-48 h before improving. The clinical signs in all thirteen surviving monkeys had generally disappeared after 7 days. In two of the three fatal cases, furthermore, the clinical signs had abated after 5-7 days. These animals subsequently became blind and died after 10 and 23 days.

The course of treatment greatly influenced the efficacy of the suppression. As long as the suppressive treatment exceeded a certain critical period (10-12 days) the animals gave no indication of a relapse up to the present time, a 6-16 month period. The animals which recovered seemed to be normal in behaviour and habits. Even in more severe cases of leg or arm paralysis, limb movement increased slowly over several weeks until normal. If successive daily injections were stopped during the critical period, permanent suppression was not achieved and clinical signs reappeared after a lapse of 3-7 days. Permanent suppression could be attained in these cases, however, if daily injections were resumed (Table 2, monkey IV).

Large infrequent injections are less effective than repeated, small, daily injections. When only one injection of A1 protein (10-30 mg) was given the animals improved temporarily, but the clinical signs of EAE reappeared after a lapse of 2-4 days. Moreover, when injections were given on alternate days over a 17-day period, the clinical signs returned after seven days (monkey III, Table 2), but in both cases, when daily injections were resumed, the animals again improved. Therefore, the course of injection must be continued over a critical period to prevent recurrence of clinical signs of EAE.

Previous studies suggest that EAE is associated primarily with cell-mediated immunological phenomena^{1,4,17,18}. Although there is evidence for humoral factors in early stages

of EAE²⁷, only a small percentage of animals with EAE show detectable antibody²⁸. If EAE is cell-mediated, the short term improvement period (24 h) observed by us can be interpreted as direct inactivation of circulating sensitized lymphocytes on encountering A1 protein antigen. The inactivation of sensitized cells by antigen is consistent with present interpretations of immune paralysis^{29,30}. This hypothesis is supported by the fact that antithymocytic serum (ALS) produces temporary improvement within 24 h in guinea-pigs with clinical signs of EAE³¹, and inhibits disease development when given soon after sensitization^{31,32}. Moreover, passive transfer of EAE by sensitized lymphocytes was abolished by pretreatment with brain tissue³³. In passive transfer of EAE, the severity of the disease is proportional to the number of cells transferred³⁴; injury to the blood brain barrier allows more rapid penetration of the CNS by sensitized cells and earlier onset of EAE³⁵. Thus it seems likely that the number of sensitized lymphocytes in the circulation is a statistically critical factor for disease expression leading to EAE.

The data reveal that a critical period of more than 10 days is necessary for achieving long lasting suppression. The direct destructive action of antigen on sensitized lymphocytes or stem cells of the central lymphoid tissue³⁶ reasonably explains these

Table 2 The Course of Suppression in Representative Monkeys with Clinical Signs of EAE *

Monkey	Day of onset	Course of suppression †	Clinical observations
I	14	Day 14: 10 mg Day 15-31: 2 mg daily	Onset: Ataxia, leg weakness, circling cage; loss of coordination 24 h: Improved Day 16: Eating, more active Day 19: Nearly normal activity, legs still weak Day 33: Seems normal
II	21	Day 21: 10 mg Day 22-32: 2 mg daily	Onset: Ataxia; anorexia, lost coordination; bumping head 24 h: Improved; eating fruit Day 23: Climbing; weak Day 28: Nearly normal, active; no ataxia, stronger Day 30: Seems normal
III	26	Day 26: 30 mg Day 27-43: 2 mg on alternate days Day 50-61: 2-4 mg daily Relapse→	Onset: Severe ataxia, anorexia, prostration, leg weakness 24 h: Improved Day 31: Eating, sitting upright, less ataxia Day 50: Severe ataxia, weakness, prostrate Day 70: Stronger, nearly normal Day 73: Seems normal
IV	18	Day 19: 10 mg Day 20-30: 2 mg daily Day 33-38: 2-4 mg daily Relapse→	Onset: Severe ataxia, anorexia, tremors, loss of coordination, severe weakness 24 h: Worse: left leg and arm paralysed Day 21: Prostrate, near death Day 23: Stronger, eating Day 29: Climbing, no ataxia; left side still weak Day 32: Anorexia, severe ataxia, left side still weak Day 35: Stronger, eating, less ataxia Day 46: Near normal, but left side weak Day 60: Left side much stronger, normal behaviour

* The other animals of this study (Table 1), which survived the suppressive treatment, had histories similar to monkeys I and II.

† Either human A1 protein or the HNB derivative was used.

results. Although it is unlikely that blocking antibody could be produced rapidly enough to account for the immediate (24 h) improvement, it should be noted that in 35% of the animals, antibody was detected after completion of the suppressive treatment. It is possible, therefore, that the long term suppression could involve blocking antibody.

Our study seems to be one of the first cases of complete reversal of an experimentally produced autoimmune disease after manifestation of definite clinical signs. With the exception of cyclophosphamide in rats³⁷, chemical agents which inhibit EAE if given near the time of sensitization cannot suppress disease if given after onset³⁸. The use of a purified, defined antigen, because of its specificity, is preferable to immunosuppressive drug therapy. Our results, therefore, may suggest a relevant clinical approach in human immunopathology, particularly in those conditions having similarities to experimental allergic encephalomyelitis.

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- ¹ Eylar, E. H., Salk, J., Beveridge, G., and Brown, L., *Arch. Biochem. Biophys.*, **132**, 34 (1969).
- ² Adams, C., and Liebowitz, S., in *The Structure and Function of Nervous Tissue* (edit. by Bourne, G.), **3**, 309 (Academic Press, New York, 1969).
- ³ Paterson, P., *Adv. Immunol.*, **5**, 131 (1966).
- ⁴ Alvord, E., in *Handbook of Clinical Neurology* (edit. by Vinken, P., and Bruyn, G.), **9**, 500 (North-Holland, Amsterdam, 1970).
- ⁵ Roboz-Einstein, E., Robertson, D., Di Caprio, J., and Moore, W., *J. Neurochem.*, **9**, 353 (1962).
- ⁶ Laatsch, R., Kies, M., Gordon, S., and Alvord, E., *J. Exp. Med.*, **115**, 777 (1962).
- ⁷ Eylar, E. H., Brostoff, S., Hashim, G., Caccam, J., and Burnett, P., *J. Biol. Chem.*, **246**, 5770 (1971).
- ⁸ Eylar, E. H., *Proc. US Nat. Acad. Sci.*, **67**, 1425 (1970).
- ⁹ Brostoff, S., and Eylar, E. H., *Proc. US Nat. Acad. Sci.*, **67**, 1425 (1970); **68**, 765 (1971).
- ¹⁰ Eylar, E. H., Westall, F., and Brostoff, S., *J. Biol. Chem.*, **246**, 3418 (1971).
- ¹¹ Kibler, R., McKneally, S., Jenkins, J., Selden, P., and Chow, F., *Science*, **164**, 577 (1969).
- ¹² Eylar, E. H., and Hashim, G., *Proc. US Nat. Acad. Sci.*, **61**, 644 (1968).
- ¹³ Eylar, E. H., Caccam, J., Jackson, J., and Robinson, A., *Science*, **168**, 1220 (1970).
- ¹⁴ Westall, F., Robinson, A., Caccam, J., Jackson, J., and Eylar, E. H., *Nature*, **229**, 22 (1971).
- ¹⁵ Eylar, E. H., Brostoff, S., Jackson, J., and Carter, H., *Proc. US Nat. Acad. Sci.* (in the press).
- ¹⁶ Dresser, D., and Mitchison, N., *Adv. Immunol.*, **8**, 129 (1968).
- ¹⁷ Paterson, P., Coia, E., and Jacobs, A., *Ann. NY Acad. Sci.*, **122**, 256 (1965).
- ¹⁸ Salvin, S., and Liauw, H., *J. Immunol.*, **101**, 33 (1968).
- ¹⁹ Alvord, E., Shaw, C., Hrubby, S., and Kies, M., *Ann. NY Acad. Sci.*, **122**, 333 (1965).
- ²⁰ Einstein, E., Csejtei, J., Davis, W., and Rauch, H., *Immunochimistry*, **5**, 567 (1968).
- ²¹ Cunningham, V., and Field, E. J., *Ann. NY Acad. Sci.*, **122**, 346 (1965).
- ²² Eylar, E. H., in *Immunologic Disorders of the Nervous System* (edit. by Rowland, L.), **5** (Academic Press, New York, 1971).
- ²³ Kabat, E., Wolf, A., and Bezer, A., *J. Exp. Med.*, **85**, 117 (1947).
- ²⁴ Oshiro, Y., and Eylar, E. H., *Arch. Biochem. Biophys.*, **138**, 606 (1970).
- ²⁵ Eylar, E. H., and Hashim, G., *Arch. Biochem. Biophys.*, **131**, 215 (1969).
- ²⁶ Barman, T., and Koshland, D., *J. Biol. Chem.*, **242**, 5771 (1967).
- ²⁷ Oldstone, M., and Dixon, F., *Amer. J. Pathol.*, **52**, 251 (1968).
- ²⁸ Seil, F., Falk, G., Kies, M., and Alvord, E., *Exp. Neurol.*, **22**, 545 (1968).
- ²⁹ Mitchison, N. A., *Transplant Proc.*, **2**, 93 (1970).
- ³⁰ Waksman, B., *Hospital Practice*, **3**, 22 (1968).
- ³¹ Liebowitz, S., Lessof, M., and Kennedy, L., *Clin. Exp. Immunol.*, **3**, 753 (1968).
- ³² Waksman, B., Arbouys, S., and Arnason, B., *J. Exp. Med.*, **114**, 997 (1961).
- ³³ Paterson, P., in *International Convocation on Immunology* (edit. by Rose, N., and Milgrom, F.), 260 (Karger, New York, 1969).
- ³⁴ Falk, G., Kies, M., and Alvord, E., *J. Immunol.*, **101**, 638 (1969).
- ³⁵ Levine, S., and Hoenig, E., *J. Immunol.*, **100**, 1310 (1968).
- ³⁶ Frey, J., De Weck, A., and Geleick, H., *Clin. Exp. Immunol.*, **8**, 131 (1971).
- ³⁷ Paterson, P., in *Immunological Diseases* (edit. by Samter, M.), 788 (Little, Brown, Boston, 1965).
- ³⁸ Paterson, P., and Drobish, D., *Science*, **165**, 191 (1969).

Effect of L-Dopa Therapy on Urinary *p*-Tyramine Excretion and EEG Changes in Parkinson's Disease

p-TYRAMINE is a normal constituent of human urine¹⁻⁸, excreted in free and conjugated forms^{2,4,8}. The level of excretion is quantitatively evaluated by separating the phenolicamine fraction (isolated by absorption onto a 'Biorad AG50W-X2' column¹) overnight in isopropylether : methyl-ethyl ketone : acetic acid : water 9 : 1 : 5 : 5 (v/v) on a Whatman No. 2 paper strip followed by conversion to the 1-nitroso-2-naphthol fluorophore and photodensitometric evaluation⁹. This procedure has shown that approximately 60% of Parkinson patients excrete more unconjugated urinary *p*-tyramine than does a control group^{4,8,10}. Food precursors rich in *p*-tyramine were shown to increase the levels of conjugated *p*-tyramine and its principal acid metabolite *p*-hydroxyphenylacetic acid (both free and bound forms)^{4,8,11}. These three metabolites increased so as to account almost stoichiometrically for the ingested amine⁴. Sterilization of the intestinal tract with neomycin and succinyl sulphathiazole in a patient with Parkinson's disease caused a considerable increase in both free and bound forms of both amine and acid⁴. These findings suggest that a proportion of conjugated *p*-tyramine and total *p*-hydroxyphenylacetic acid arise from exogenous sources whereas most of the free urinary *p*-tyramine is endogenous⁸. This observation is confirmed in the work of several others⁵⁻⁷ although Perry *et al.*⁷ interpret their findings differently. A more convincing demonstration of the validity of our hypothesis followed from an assessment of the urinary free and bound *p*-tyramine and *p*-hydroxyphenylacetic acid excreted in urine after oral and intravenous administration of *p*-hydroxyphenyl(ethylamine-2-¹⁴C)-hydrochloride. In a control population only a tiny proportion of ingested *p*-tyramine, even when substantially supplemented with cold amine, is excreted in the urine in the free form (Table 1). After intravenous injection, however, a variable but significant amount of unconjugated amine is excreted.

The observation that the excretion of urinary dopamine is reduced in Parkinson patients¹² and that the amines dopamine, noradrenaline and serotonin are much reduced in the basal ganglia¹³ led to the introduction of the precursor substance L-dopa—presumably as a replacement chemotherapy—apparently with good results in a proportion of cases¹⁴.

We have analysed the urinary excretion levels of unconjugated *p*-tyramine and tryptamine and the electroencephalogram (EEG) record in a group of Parkinson patients undergoing clinical trials on the efficacy of L-dopa treatment. Patients, representing a broad variety of cases usually with a high degree of severity, were withdrawn from all previous anti-Parkinson drugs for the 2 weeks before admission to hospital. Urine samples (24-h), EEG assessment (see refs. 15 and 16 for further details on the techniques of quantitative integrated EEG analysis, mean integrated amplitude (MIA) and co-efficient of variation (CV)), clinical ratings and various assessments of motor ability were obtained on day 2 or 3 after admission. L-Dopa administered over a 4-6-week period was increased gradually according to clinical response and the appearance of side effects up to a final level in the range 1.5-6 g daily. Analyses were repeated at that point where considerable improvement had occurred or just before termination of the therapy because of the appearance of undesirable side effects or lack of clinical improvement.

Table 1 Urinary Excretion of *p*-Tyramine and *p*-Hydroxyphenylacetic Acid (Free and Conjugated Forms) in a Control Population after Oral and Intravenous Administration of ^{14}C -*p*-Tyramine Hydrochloride*

	<i>p</i> -Tyramine † (% of dose)		<i>p</i> -Hydroxyphenylacetic acid † (% of dose)	
	Free	Conjugated	Free	Conjugated
Oral ingestion ‡ (19 μCi , 76 μg) ($n=8$)	0.05 $\pm$ 0.023¶	0.64–1.84**	50.0–72.6**	2.0–4.5**
Supplemented oral ingestion‡ (19 μCi , 76 μg ; 100 mg cold tyramine) ($n=7$)	0.12 $\pm$ 0.074¶	0.94–4.0**	59.3–73.5**	0–7.5**
Intravenous injection§ (5 μCi , 20 μg) ($n=5$)	1.94–4.10**	0.40–1.70**	42.0–80.2**	Nil

* *p*-Hydroxyphenyl(ethylamine-2- ^{14}C)-hydrochloride (s.a. 44 mCi/mmol), (Amersham/Searle, Don Mills, Ontario).

† Corrected for recovery.

‡ Amounts shown dissolved in water.

§ Amount shown dissolved in physiological saline.

¶ Mean $\pm$ standard deviation.

** Range of values obtained.

Table 2 Effect of L-Dopa Ingestion on the Urinary Excretion of Unconjugated *p*-Tyramine and Tryptamine in a Control Group

Excretion in a control population	<i>p</i> -Tyramine 312 $\pm$ 162 † ($n=31$)			Tryptamine 83 $\pm$ 36 † ($n=16$)		
Excretion during ingestion of L-dopa	Before *	During *	After *	Before *	During *	After *
Subject 1	225 $\pm$ 30 ($n=6$)	408 $\pm$ 151 ($n=4$)	342 $\pm$ 57 ($n=4$)	56 $\pm$ 22 ($n=6$)	96 $\pm$ 22 ($n=4$)	62 $\pm$ 8 ($n=4$)
Subject 2	300 $\pm$ 86 ($n=4$)	264 $\pm$ 71 ($n=5$)	202 $\pm$ 56 ($n=2$)	107 $\pm$ 15 ($n=2$)	96 $\pm$ 18 ($n=5$)	56 $\pm$ 10 ($n=2$)
Subject 3	1,330 $\pm$ 1,380 ($n=5$)	921 $\pm$ 1,005 ($n=4$)	2,265 $\pm$ 1,957 ($n=2$)	49 $\pm$ 11 ($n=3$)	62 $\pm$ 16 ($n=4$)	44 $\pm$ 5 ($n=2$)

Subjects 1 and 3 ingested 2 g day $^{-1}$ for 4 weeks, subject 2 ingested 3 g day $^{-1}$ for 4 weeks.* Mean $\pm$ mean deviation.† Mean $\pm$ standard deviation.All data, corrected for recovery, expressed in $\mu\text{g/g}$ creatinine.Tryptamine was analysed according to the procedure described by Udenfriend 29 .

The effect of orally ingested L-dopa on the excretion of unconjugated *p*-tyramine and tryptamine in twenty-eight Parkinson patients and three control individuals is shown in Tables 2 and 3. In spite of the large variations in excretion levels of *p*-tyramine and tryptamine in the three control subjects a general decrease as was the case for some Parkinson patients (Tables 3 and 4) did not occur. Subject 3 is rather rare in the sense that on occasions his urinary *p*-tyramine excretion was very high (note the wide deviation in the listed values).

Table 3 Effect of L-Dopa Ingestion on the Urinary Excretion of Unconjugated *p*-Tyramine and Tryptamine in Parkinsonism

	Before * †	During * †
<i>p</i> -Tyramine ($n=28$)	500 $\pm$ 725 ‡	152 $\pm$ 120 §
Tryptamine ($n=27$)	72 $\pm$ 44	66 $\pm$ 36

* Values obtained on day 2 or 3 after hospital admission and then at optimum dose of L-dopa before discharge or termination (see text).

† Results, corrected for recovery, expressed in $\mu\text{g/g}$ creatinine, mean $\pm$ standard deviation.

‡ Range of values 75–2,910.

§ Range of values 21–555.

In Parkinsonism (Table 3) (in spite of the wide ranges involved) there is a significant ($P < 0.05$) decrease in the urinary excretion of unconjugated *p*-tyramine during L-dopa therapy but no significant change in the tryptamine excretion. An examination of the *p*-tyramine data indicated that some patients ($n=17$) exhibited a decrease in their excretion of this amine while others ($n=11$) did not. Splitting the group on this basis revealed (Table 4) that the patients exhibiting a decrease in their free *p*-tyramine excretion started off as high

excretors whereas the patients who either did not change, or slightly increased, were low excretors before the start of the L-dopa treatment. In neither group was there a significant change in the excretion pattern of free tryptamine which remained approximately the same as for a normal population. A fact of some interest is that none of the patients metabolized intravenously injected ^{14}C -tyramine differently from the control group represented in Table 1. A detailed description of the EEG changes will be reported fully elsewhere; briefly, L-dopa therapy produced a "normalization" of the EEG record involving considerable reductions in the amount of diffuse delta and theta frequencies and an increase in the

Table 4 Effect of L-Dopa Ingestion on the Urinary Excretion of Unconjugated *p*-Tyramine and Tryptamine in Parkinson Patients divided according to whether their *p*-Tyramine Levels Decreased or Not

	<i>p</i> -Tyramine †		Tryptamine †	
	Before *	During *	Before *	During *
Patients exhibiting a decreased excretion	726 $\pm$ 820 ‡ ($n=17$)	125 $\pm$ 108 § ($n=17$)	70 $\pm$ 33 ($n=16$)	61 $\pm$ 22 ($n=16$)
Patients exhibiting no decrease	161 $\pm$ 54.5 ($n=11$)	192 $\pm$ 132¶ ($n=11$)	72 $\pm$ 56 ($n=11$)	76 $\pm$ 43 ($n=11$)

* Values obtained on day 2 or 3 after hospital admission and then at optimum dose of L-dopa before discharge or termination (see text for further details).

† Results, corrected for recovery, expressed as $\mu\text{g/g}$ creatinine, mean $\pm$ standard deviation.

‡ Range of values 174–2,910.

§ Range of values 21–416.

¶ Range of values 77–555.

Table 5 Rank Order Correlations between the Change in the Excretion of Urinary *p*-Tyramine and Some EEG Measures

	Post-surgical (<i>n</i> = 11)	Non-surgical (<i>n</i> = 12)	All patients (<i>n</i> = 23)
MIA decrease	0.13	-0.19	-0.08
CV increase	0.67 *	0.41	0.39 *

* Significant at the 95% confidence level.

alpha frequency content. From integrated EEG measures it was apparent that before the drug treatment signal variability (CV scores) extended down to extremely low values, even lower in fact than those seen in chronic withdrawn schizophrenics or hallucinating acute schizophrenics. The MIA tended to be higher and the CV significantly lower than normal values. The changes occurring during L-dopa therapy were different depending on whether the patient had previously undergone brain surgery. In the non-surgical cases (*n* = 27) the CV scores increased, while in all cases (*n* = 40) the MIA scores decreased. Significant correlations were observed between increases in CV and decreases on the Columbia Scale of Disability¹⁷; changes in the tremor ratings correlated significantly with decreases in MIA and increases in CV.

In patients where both EEG and amines were analysed (*n* = 23) a significant correlation (Table 5) existed between increases in CV and decreases in urinary *p*-tyramine excretion. In post-surgical cases this correlation was even more marked. This is not the first time that a correlation between the EEG and urinary unconjugated *p*-tyramine has been observed. In a heterogeneous population of schizophrenic patients a significant correlation existed between those patients exhibiting abnormalities in their EEG and above normal levels of urinary *p*-tyramine⁸.

It is a puzzle that urinary free *p*-tyramine should decrease during L-dopa treatment while tryptamine remains relatively unchanged. If the amines were formed simply by decarboxylation of their parent amino-acids recently available kinetic data on the responsible enzyme—L-aromatic amino-acid decarboxylase—indicate that tryptophan would be much more easily decarboxylated¹⁸ than *p*-tyrosine. If the newly discovered enzyme, dopamine dehydroxylase¹⁹, were involved it might be expected that *p*-tyramine excretion would increase on account of the high levels of circulatory L-dopa and hence presumably dopamine. It is quite possible that dopa, dopamine or one of the recently postulated products of dopa metabolism²⁰ might act as an inhibitor of one or both of the above mentioned enzymes as is the case, for example, between dopa and tyrosine aminotransferase²¹.

The recent identification of *p*-tyramine and other non-catecholic amines (octopamine, phenylethylamine and tryptamine) in rat²²⁻²⁴ and human brain²⁵, and the demonstration that *p*-tyramine is present in significant quantities and distributed similarly to noradrenaline in both the rat and man²⁵, suggest that this particular amine (and probably the others) possesses some neurophysiological role. The observed low levels, in Parkinson patients, of dopamine in the urine and basal ganglia and the increased urinary level of *p*-tyramine together with the recent identification of cerebral dehydroxylation of dopamine to *p*-tyramine and the results contained in this paper seem to suggest an involvement of *p*-tyramine in the aetiology of Parkinsonism at least in a proportion of cases. Recent mass spectrometric analyses have shown that rat brain tyramine is almost, if not entirely, the *para* isomer²⁶. This means that it is the *meta* hydroxyl group that is lost from dopamine during dehydroxylation so that little, if any, *meta* tyramine can be present. Although this latter observation is so far confined to the rat, it is important in view of the recent suggestion by Sandler *et al.*^{27,28} that perhaps in Parkinsonism intestinal *para* dehydroxylation of dopa occurs with the resultant *meta* tyrosine being transported to the brain where it is converted to *meta* tyramine; this then acts to protect dopamine.

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- ¹ Kakimoto, Y., and Armstrong, M. D., *J. Biol. Chem.*, **237**, 208 (1962).
- ² Boulton, A. A., Pollitt, R. J., and Majer, J. R., *Nature*, **215**, 132 (1967).
- ³ Smith, I., and Kellow, A. H., *Nature*, **221**, 1261 (1969).
- ⁴ Boulton, A. A., *Prog. Neurogenetics*, **1**, 437 (1967).
- ⁵ Asatoor, A. M., *Clin. Chim. Acta*, **22**, 223 (1968).
- ⁶ DeQuattro, V. L., and Sjoerdsma, A., *Clin. Chim. Acta*, **16**, 227 (1967).
- ⁷ Perry, T. L., Hestrin, M., MacDougall, L., and Hansen, S., *Clin. Chim. Acta*, **14**, 116 (1966).
- ⁸ Boulton, A. A., Marjerrison, G. L., and Majer, J. R., *Symp. Clin. Biol. Res. Schizophrenia*, Leningrad (September 1970, in the press).
- ⁹ Boulton, A. A., *Meth. Biochem. Anal.*, **16**, 327 (1968).
- ¹⁰ Marjerrison, G. L., Boulton, A. A., and Rajput, A., *Intern. J. Clin. Pharmacol.*, **4**, 263 (1971).
- ¹¹ Boulton, A. A., in *L-Dopa and Parkinsonism* (edit. by Barbeau, A., and McDowell, F. H.) (F. A. Davis, Philadelphia, 1970).
- ¹² Barbeau, A., Murphy, G. F., and Sourkes, T. L., *Science*, **133**, 1706 (1961).
- ¹³ Hornekyewicz, O., *Pharmacol. Rev.*, **18**, 925 (1966).
- ¹⁴ Cotzias, G. C., in *L-Dopa and Parkinsonism* (edit. by Barbeau, A., and McDowell, F. H.) (F. A. Davis, Philadelphia, 1970).
- ¹⁵ Goldstein, L., Sugerman, A. A., Stolberg, H., Murphree, H. B., and Pfeiffer, C. C., *EEG Clin. Neurophysiol.*, **19**, 350 (1965).
- ¹⁶ Marjerrison, G. L., Krause, A. E., and Keogh, R. P., *EEG Clin. Neurophysiol.*, **24**, 35 (1968).
- ¹⁷ Yahr, M. D., Duvoisin, R. C., Schear, M. J., Barrett, R. E., and Hoehn, M. M., *Arch. Neurol.*, **21**, 343 (1969).
- ¹⁸ Christenson, J. G., Pairman, W., and Udenfriend, S., *Arch. Biochem. Biophys.*, **141**, 356 (1970).
- ¹⁹ Boulton, A. A., and Quan, Lillian, *Canad. J. Biochem.*, **48**, 1287 (1970).
- ²⁰ Sourkes, T. L., *Nature*, **229**, 413 (1971).
- ²¹ Fellman, J. H., and Roth, E. S., *Biochemistry*, **10**, 408 (1971).
- ²² Boulton, A. A., and Majer, J. R., *Nature*, **225**, 658 (1970).
- ²³ Majer, J. R., and Boulton, A. A., *J. Chromatog.*, **48**, 322 (1970).
- ²⁴ Boulton, A. A., and Majer, J. R., *Methods in Neurochemistry*, **1** (edit. by Rodnight, R., and Marks, N.) (Plenum, New York, in the press).
- ²⁵ Majer, J. R., and Boulton, A. A., *Meth. Biochem. Anal.*, **49**, 993 (1971).
- ²⁶ Boulton, A. A., and Majer, J. R., *Canad. J. Biochem.* (in the press).
- ²⁷ Sandler, M., Karoun, F., Ruthven, C. R. J., and Calne, D. B., *Science*, **166**, 1417 (1969).
- ²⁸ Sandler, M., Goodwin, B. L., Ruthven, C. R. J., and Calne, D. B., *Nature*, **229**, 414 (1971).
- ²⁹ Udenfriend, S., in *Fluorescence Assay in Biology and Medicine*, 164 (Academic Press, New York, 1962).

Australia Antigen as a Marker of Propagation of the Serum Hepatitis Virus in Liver Cultures

ATTEMPTS to isolate the human hepatitis viruses in tissue culture have resulted in a collection of "hepatitis-candidate" viruses, none of which has since been shown to be the causal agent of human hepatitis¹. The discovery of Australia antigen provided a specific serological marker of infection with or carriage of the serum hepatitis virus, although the nature of the antigen remains unsettled².

Preliminary observations on the irregular production of cytopathic changes by purified fractions of serum containing

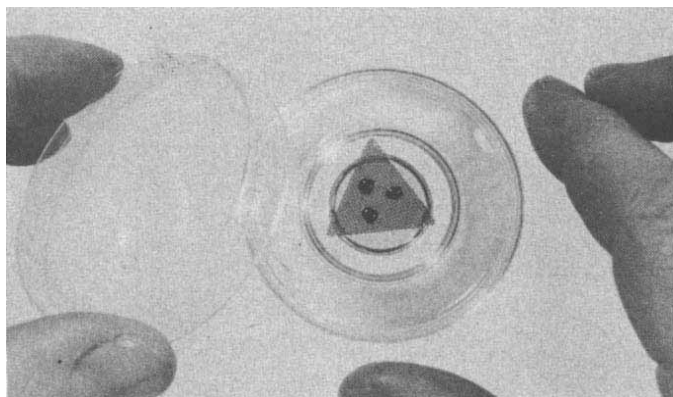


Fig. 1 Organ culture of human embryo liver 24 h after preparation.

Australia antigen in monolayer cultures of differentiated human embryo liver cells³ proved unpredictable. More recently, however, the induction of progressive changes in such cultures has been reported after inoculation with a known infective hepatitis serum. There was progressive involvement of the normal cellular components of the cultured liver cells, as demonstrated by specific fluorescent antibody attachment, first in the cytoplasm, then in the perinuclear membrane and finally condensation in the nucleoli. Similar progressive changes have been observed in cells of liver cultures inoculated with supernatant fluid which has been passaged in culture once⁴. Virtually identical fluorescent changes have been reported in liver cells cultured from biopsy material obtained from a patient with circulating Australia antigen. After six passages of the cells, the cultured cells still contained Australia antigen in the nuclei and the antigen was also detected by radioimmunoassay in the supernatant fluid⁵.

More reliable changes can be obtained, however, by using small fragments of tissue maintained in synthetic media as organ cultures. These can be used to propagate certain viruses that are difficult to grow in conventional cell cultures. A technique has now been developed for maintaining human embryo liver organ cultures for at least 10 days. These cultures support the growth of type 3 adenovirus⁶, and they have been used for the inoculation of serum specimens from patients and carriers of type B viral hepatitis with some encouraging results⁷.

Human livers, obtained after abdominal hysterotomy, from 10–16-week-old embryos were prepared for organ culture as soon as possible after dissection, usually within 3–4 h. The tissue was washed in Hanks balanced salt solution and cut into fragments of approximately 2 cm³. Three fragments were placed on sterilized stainless steel grids, which fit into the centre well of a Falcon disposable plastic organ culture dish (Fig. 1). Eagle's minimum essential medium with 0.2% bovine serum albumin, 100 U of penicillin, 100 µg of streptomycin and 50 U of 'Nystatin' ml.⁻¹, was added to the centre well until the tissue was bathed but not immersed in the medium (0.8 ml.). The pH of the medium was maintained at 6.8 and the cultures incubated at 35° C. A sample of 0.1 ml. of serum from three different sources was used for inoculation. Serum P.J.G. was obtained from a former blood donor who was implicated in three cases of serum hepatitis. His serum was shown to be infective by volunteer studies and Australia antigen has been demonstrated repeatedly in his serum⁸. Serum R.B. was collected from a jaundiced patient admitted to a London hospital with viral hepatitis and Australia antigen was subsequently detected serologically. Serum G.C. was obtained from an apparently healthy volunteer blood donor whose blood had caused two deaths from post-transfusion hepatitis in transfused recipients. Australia antigen was demonstrated in this serum by routine serological tests and by electron microscopy.

The inoculated sera were incubated with the organ cultures

for 72 h at 35° C. The culture fluid was removed with a fine pipette, replaced with fresh medium and the incubation continued. The culture fluid together with the liver fragments were collected after 6 and 8 days. The material was then rapidly frozen and thawed three times and the resulting fluid used for examination for Australia antigen. The antigen could not be demonstrated in the supernatant fluid by immunodiffusion, complement fixation or radioimmunoassay after 3 days of incubation. Progressive rise in the titre of Australia antigen was obtained with serum G.C. and serum R.B., from a complement fixing titre of 1:4 at 6 days to 1:128 after

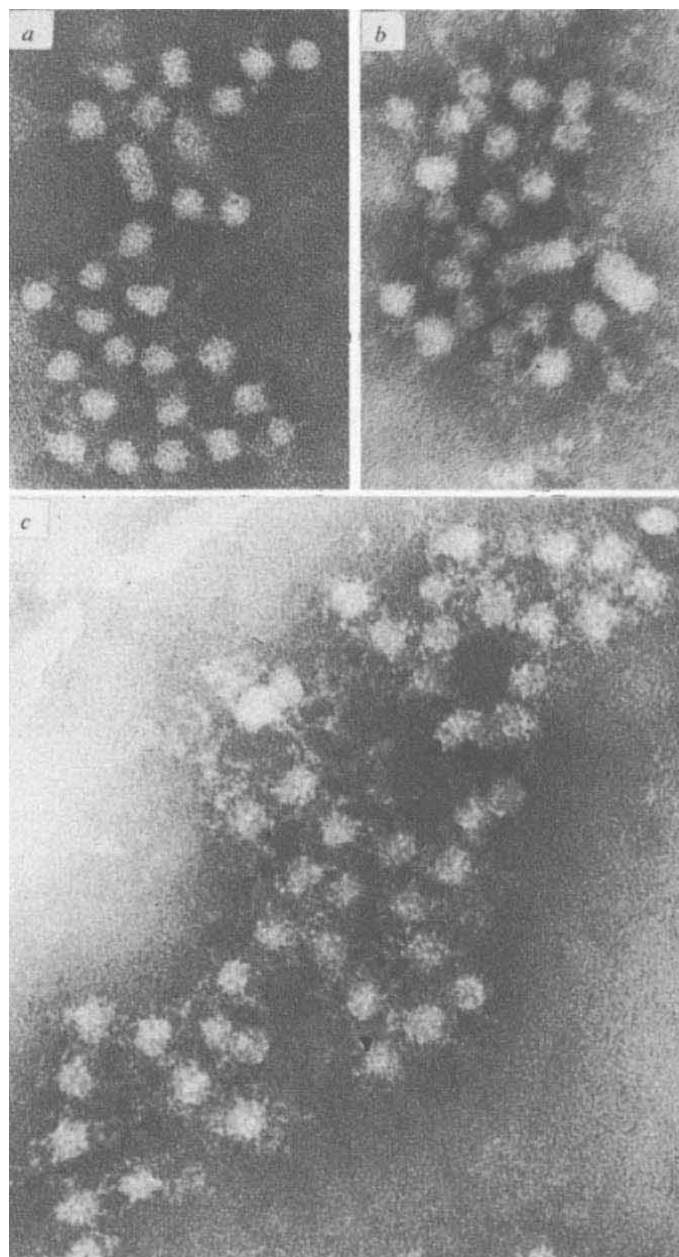
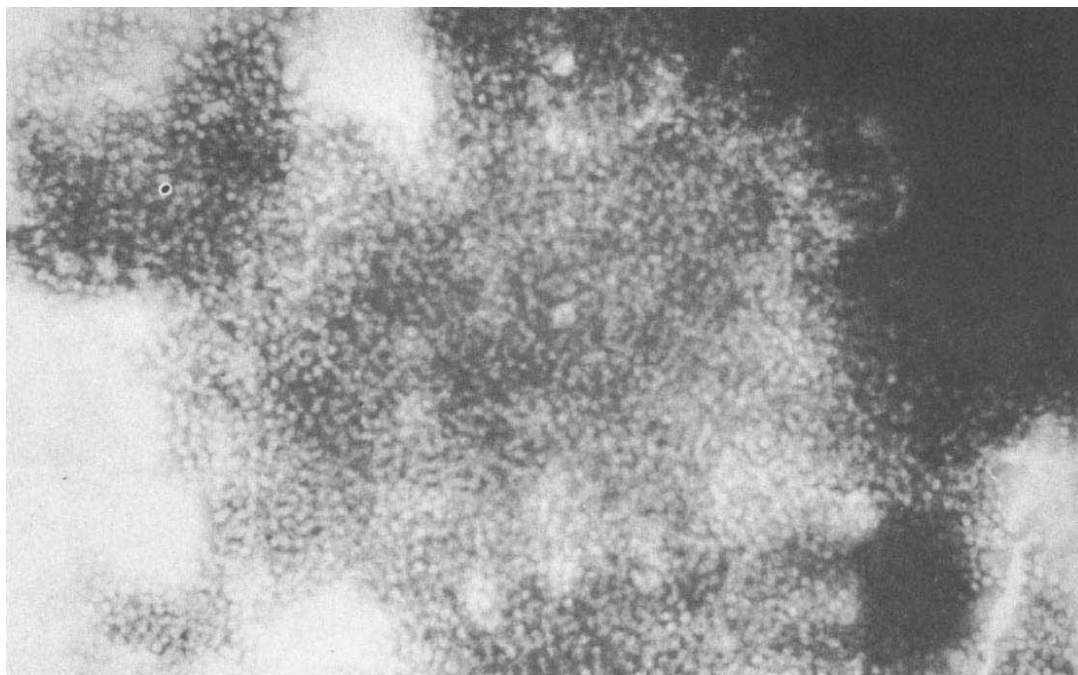


Fig. 2 *a*, A small aggregate of Australia antigen particles present in the serum of R.B. This patient had clinical serum hepatitis and the serum was one of the three sera used for inoculation of the organ cultures ($\times 300,000$). *b*, This micrograph was obtained from the organ culture fluid 6 days after inoculation with the serum shown in Fig. 2*a*. Only very occasional small aggregates of the type shown here were found ($\times 300,000$). *c*, After 8 days growth in organ culture, examination of the culture fluid in the electron microscope revealed numerous aggregates showing the typical morphology of Australia antigen. The aggregate illustrated here has been chosen because it is possible to see bridging of the particles by antibody present in a serum containing specific anti-Au globulin ($\times 300,000$).

Fig. 3 Using as inoculum the material harvested from the experiment illustrated in Fig. 2c, an additional pass in organ culture was carried out. At day 8 of this first passage the electron microscope revealed the presence of enormous numbers of particles having the typical morphology of Australia antigen and aggregated by antibody specific to it. The micrograph shows only the thin edge of an aggregate which was itself 3 μ m in diameter ($\times 80,000$).



8 days in culture. In the two dimensional micro-Ouchterlony technique there was an increase in precipitin titre from 0 at 6 days to 1 : 4 on day 8.

The specimens for electron microscopy were fluids from organ cultures containing considerable amounts of cell debris, so we looked for aggregates of antigen rather than individual particles⁹. This was achieved by adding 0.1 ml. of a 1 : 5 dilution of haemophilic serum, known to contain specific antibody to the Australia antigen, to 0.5 ml. of the organ culture fluid. The tubes were then incubated for 30 min at 37° C and centrifuged for 1 h at 18,000 r.p.m. in a Sorvall RC2b centrifuge. The supernatant was discarded and the pellets used for negative staining as follows. Immediately before examination the pellet was resuspended in approximately 0.1 ml. of distilled water and an aliquot of this mixed with an equal quantity of 3% phosphotungstic acid adjusted to pH 6.0. A drop of this mixture was then placed on a 400 mesh carbon-formvar coated grid and examined in a Philips EM 300, chiefly at a plate magnification of $\times 60,000$.

In each of the three sera used were found the particles now associated with Australia antigen. In each case the addition of antiserum had clumped the particles and direct bridging by antibody molecules could be seen (Fig. 2c). Tissue culture material from control specimens contained numerous small particles in the size range of the 200 Å diameter Australia antigen particles. These particles, however, were never clumped by antibody and on closer examination appeared to be the normal constituents of any tissue culture preparation. On the sixth day of the original cultures, which were infected with G.C. and R.B., the electron microscope revealed that a small number of aggregates built up with typical Australia antigen particles were present. These immune aggregates were small and could be found only by diligent searching (Fig. 2b). By day 8 of this series, the grids examined contained numerous large aggregates again typical of Australia antigen particles. The aggregate shown in Fig. 2c has been chosen for illustration because it is possible to see the antibody linkage by specific anti-Au serum.

The control preparations and cultures inoculated with a normal serum remained negative by all serological tests and on electron microscopic examination.

The fluid collected from the 8 day cultures inoculated with G.C. and R.B. was passaged into fresh organ cultures. There was no detectable complement fixing activity in the tissue fluid collected after 6 days and only a slight rise in the comple-

ment fixing titre to 1 : 2 with the G.C. passage material at 8 days. The immunodiffusion test both on the sixth and eighth day was negative. No complement fixing nor precipitin reactions were detected in the sixth day collection from R.B. passage material. On the other hand, although complement was fixed to a titre of only 1 : 4 at 8 days with R.B. passage material, a sharply defined precipitin line was obtained in the gel diffusion test, showing a line of immunological identity with known reference Australia antigen-containing sera.

The day 6 passage material derived from G.C. showed very scanty aggregates in the electron microscope, and in the specimen from day 8 there was only a very small increase in the number of Australia antigen particles. Similarly, day 6 of the first passage material derived from R.B. revealed only small scattered aggregates of Australia antigen; but on day 8 the specimen was found to contain considerably more Australia antigen than had been seen in any of the previous specimens including the original starting material. Many of the aggregates were too large for high resolution microscopy and the aggregate shown in Fig. 3 is a thinly spread area at the edge of an aggregate, which was approximately 3 μ m in diameter.

It is interesting that although occasional 420 Å (Dane) particles¹⁰ could be found in the original inocula these were not seen in any of the cultured specimens. On the other hand, the specimens contained approximately 200 Å diameter spheres and tubules that are typical of the Australia antigen.

The passage controls and serum negative controls were entirely negative by complement fixation, immunodiffusion, electron microscopy and radioimmunoassay. The low complement fixing titres of the R.B. passage material, in the presence of marked positive precipitin reactions and numerous Australia antigen particles revealed by immune electron microscopy (Fig. 3), suggest that complement fixing activity of Australia antigen is considerably reduced after adaptation to tissue culture conditions. Further serial passages are in progress.

Finally, there was no detectable rise in the complement-fixing titre nor a precipitin reaction for Australia antigen after inoculation of the third serum from P.J.G., nor on passage⁷.

Australia antigen is generally recognized as a specific marker of infection with serum hepatitis virus. We conclude therefore that apparent replication of the serum hepatitis virus, as far as it can be based on measurement of Australia antigen, has taken place in organ cultures of human liver. The difficulty in obtaining suitable human foetal liver and the variation

associated with primary tissues of different sources and ages may limit the large scale use of our culture technique. The human coronaviruses, however, were initially only capable of growth in organ culture, but after a period of adaptation by this means they could be grown on standard continuous cell cultures. It may be that a period of adaptation on foetal liver organ cultures could produce the same effect for the virus of serum hepatitis.

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- ¹ Zuckerman, A. J., *Virus Diseases of the Liver*, 46 (Butterworth, London, 1970).
- ² Memorandum: Tests for Australia (hepatitis-associated) antigen and antibody, *Bull. Wld Hlth Org.*, **42**, 957 (1970).
- ³ Zuckerman, A. J., *Nature*, **223**, 569 (1969).
- ⁴ Brighton, W. D., Taylor, P. E., and Zuckerman, A. J., *Nature New Biology*, **232**, 57 (1971).
- ⁵ Coyne, V. E., Millman, I., and Blumberg, B. S., *Bacteriol. Proc.* (Abstr.), 175 (1971).
- ⁶ Baines, P. M., Taylor, P. E., and Zuckerman, A. J., *Arch. Ges. Virusforsch.* (in the press).
- ⁷ Zuckerman, A. J., *Vox Sang.*, **19**, 304 (1970).
- ⁸ Zuckerman, A. J., and Taylor, P. E., *Nature*, **223**, 81 (1969).
- ⁹ Almeida, J. D., and Waterson, A. P., *Adv. Virus Res.*, **15**, 307 (1969).
- ¹⁰ Dane, D. S., Cameron, C. H., and Briggs, M., *Lancet*, **i**, 695 (1970).

New Semi-dominant Mutation in the Syrian Hamster

SEVERAL different mutations causing hypotrichosis are well known in both rats and mice^{1,2} but none have so far been described in the hamster.

In November 1968 a spontaneous semi-dominant mutation causing hypotrichosis occurred in a litter of hamsters (*Mesocricetus auratus*) maintained by one of us (M. K. W.). A single male animal with a "sparse coat" was noted among normal littermates. The mating was repeated twice, but no further abnormal young were observed.

The mutant male was mated to normal females of the same strain, and approximately 50% of his offspring had a sparse coat. The original male was then mated to his sparse-coated daughters, and in May 1969 the first hairless young were observed. Breeding data given in Table 1 indicate that the condition is caused by an autosomal semi-dominant mutation resembling "naked" in the mouse. Because of this resemblance,



Fig. 1 The naked hamster.

the name "naked" with the gene symbol *N* is proposed for this mutant.

Homozygous naked hamsters are completely devoid of hair apart from a very short and soft down (Fig. 1). Vibrissae are present but are soft and tend to be bent. Naked hamsters which reach weaning age are viable, though they have a reduced body weight, and are probably more sensitive to environmental factors than normal hamsters. Both male and female homozygotes are fertile though the few females that have produced young have so far been unable to rear them. The breeding data shown in Table 1 indicate that there is about a 30% deficiency of homozygotes at weaning, thus the effect on viability is much less marked than the naked mutant in the mouse³.

The onset of the condition has not been studied in detail, but naked individuals are identifiable at about 14 days of age, and there is no evidence of hair growth from then onwards. Heterozygotes are identifiable from about 14 days of age onwards by their sparse coat, which is particularly deficient on the ventral surface, though the nature of the deficiency has not yet been determined. Microscopic examination of hair clippings from heterozygotes reveals no obvious deficiency in either type or diameter of the hairs. Viability and breeding performance of the heterozygotes are normal, though there may be a slight reduction in body weight.

According to Kirkman and Algard⁴ the epidermis of the hamster is responsive to a variety of chemical carcinogens, producing the same types of tumours as other laboratory animals. The naked hamster may prove useful in studies of such neoplasia as it eliminates the need to shave the hamsters before applying the carcinogen.

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¹ Robinson, R., *Genetics of the Norway Rat* (Pergamon Press, London, 1965).

² Green, E. L., *Biology of the Laboratory Mouse* (McGraw-Hill, New York, 1966).

Table 1 Breeding Results

Mating		No. litters born	Young weaned		
♀	♂		+/+	N/+	N/N
+/+ × +/+		5	38	—	—
+/+ × +/N		22	95	81	—
+/N × +/N		26	60	98	39
+/N × N/N		15	—	61	42
+/+ × N/N		8	—	65	—
N/N × N/N		2	None	None	None

³ Gruneberg, H., *The Genetics of the Mouse* (Martinus Nijhoff, The Hague, 1952).

⁴ Kirkman, H., and Algard, F. T., *The Golden Hamster* (edit. by Hoffman, R. A., Robinson, P. F., and Magathas, H.) (Iowa State University Press, Ames, 1968).

Phloem Physiology and Protective Sealing Mechanisms

RECENTLY Dr Spanner, in a review "Transport in the Phloem"¹, described certain aspects of my work² but reinterpreted my reported observations in accordance with his scheme to explain the mechanism of phloem transport. His description that the massage pretreatment applied to *Ricinus* stems in my experiments was "gentle" is not correct. The theory behind the method is to compress phloem sieve tubes containing sap under pressure of about 10 bar, so as to make it surge rapidly along the tubes; manual pressure was applied firmly though not so as to produce detectable damage during the application. Similarly the brief application of quite strong pressure is needed to stop exudation completely.

He describes as "contrived" my proposals for the sieve plates as control systems, governed by sealing and anti-sealing mechanisms, in view of the "obvious" alternative that the pretreatment merely disrupts the natural system. Yet callose deposition, one accepted sieveplate sealing mechanism, is known to be reversible³. Further evidence supporting my theory will be published shortly⁴ in which illustrations of the complexity of the sealing system are presented. For example, a cut may exude, then stop completely for a time, begin again without interference and finally cease (the "re-bleed phenomenon"), which defies a simple explanation.

A further important finding is that *Ricinus* plants may exude considerable amounts of sap without pretreatment if they are grown sufficiently vigorously⁵. Such exudation can also be stopped by the temporary application of pressure. More than 3 ml. of phloem exudate has been collected from a single 5 mm cut in an unmassaged plant about 50 cm tall (Baker and Hall, unpublished result), whereas the corresponding maximum on record from a single cut in a vigorous massaged plant is now more than 10 ml. This rapid collection of phloem sap from plants in amounts too large to be accounted for by turgor release from single cells is a most serious obstacle to acceptance of an "occluded pore" mechanism. Not only is massage pretreatment inessential, but the amounts collected above and below cuts are in roughly equal amounts as one might expect of a simple pressure release. We should expect the output from a pumping system between leaves and roots to be polarized and produce dissimilar amounts.

It is surprising that the palm sugar industry, which produces thousands of tons of sugar annually from phloem exudate⁶, has been so ignored by plant physiologists. It was from Bose's account⁷ of the collection system that my successful massage pretreatment was devised. There are local variations in technique but my enquiries into these have been curtailed by the Pakistan troubles. But an eyewitness, Mr Syed Hadiuzzaman of Dacca University, has described a method for the collection of *Phoenix* phloem sap without massage pretreatment, by "V" shaped incisions alone. Experts incise the upper trunks after removal of a series of leaf bases, which otherwise protect the tissues from injury. Cuts are renewed every few days and provide several litres of sap (about 14% sucrose) per day. Thus it seems that the mechanisms involved are similar in *Phoenix* and *Ricinus* and pretreatment by "disruptive" massage is not essential for exudation from either.

In terms of evolutionary development it can be argued^{3,4} that such a rich potential food supply as phloem has become adapted to seal rapidly to withstand the onslaught of predators. Probably this has been largely achieved. Exceptions are small insects, for example aphids, which probably tap the sieve tubes at rates too slow to trigger the sealing response³, and

larger animals, for example the sapsucker, a bird which makes a succession of wounds so bypassing blocked tissues⁸. If man can succeed where most animals would fail, large resources of sugars, amino-acids and proteins should become available "on tap" from otherwise useless vegetation.

A serious problem in studying phloem physiology has been the difficulty of establishing if tissue is still capable of conduction after being treated experimentally. The sensitivity of the tissue to manipulation is now beyond question. If sieve plates have become adapted to seal rapidly, this probably explains why considerable efforts, using largely empirical techniques, to demonstrate "open" sieve plate pores have produced inconclusive or controversial results.

If the explanation proposed is correct the most efficient way to prove the mechanism of phloem transport is to elucidate further the physiology of the sealing mechanisms with a view to controlling them. We now have plants in which the system can be studied systematically (*Yucca*⁹, *Phoenix*, and *Ricinus*) and only when the sealing mechanisms are fully understood will it be possible to demonstrate convincingly the ultra-structure of sieve plate pores in the natural state.

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DR SPANNER writes: I am grateful to Dr Milburn for correcting the wrong impression given by my use of "gently". Further thought on his interesting results inclines me to greater sympathy with his view. My reaction had been to conclude that his metabolic sealing-antisealing mechanism had involved P-protein, a conclusion against which strong arguments have been raised¹. If he is thinking rather of callose formation I find his suggestions plausible. But in that case they seem to me to lose their relevance to the controversy about whether the sieve plate pores are normally occupied by P-protein, as my Fig. 1 indicated¹⁰. One only has to assume that the usual brevity of exudation hinges on the formation of callose rather than on the filling of the pores with P-protein to see this. For I believe that the electro-osmotically significant P-protein in the pores does not require very much force to displace it. (I am not thinking, of course, of massive protein plugs in the lumen.) Consequently the situation at the cut surface is dominated by the huge turgor gradient, and pays little attention to whether the pores are normally open or occluded. That exudation from the two surfaces of the cut should be more or less equal (not always found incidentally¹¹) is understandable. Similarly the re-bleed phenomenon does not seem so hard to explain; pressure build-up might dislodge a proteinaceous accumulation at a callose-constricted sieve plate.

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¹ Spanner, D. C., *Nature*, **232**, 157 (1971).

² Milburn, J. A., *Planta*, **95**, 272 (1970).

³ Zimmermann, M., in *Physiology of Plant Growth and Development* (edit. by Wilkins, M. B.), 383 (McGraw-Hill, London and New York, 1969).

⁴ Milburn, J. A., *Planta*, **100**, 143 (1971).

⁵ Hall, S. M., Baker, D. A., and Milburn, J. A., *Planta*, **100**, 200 (1971).

⁶ Schery, R. W., *Plants for Man*, 346 (Allen and Unwin, London, 1954).

⁷ Bose, J. C., *Plants and their Autographs*, 154 (Longmans, Green and Co., London, 1947).

⁸ Crafts, A. S., *Translocation in Plants*, 97 (Holt, Rinehart and Winston, New York, 1961).

⁹ Tammes, P. M. L., and Die, J. van, *Acta Bot. Neerl.*, **13**, 76 (1964).

¹⁰ Spanner, D. C., *Nature*, **232**, 157 (1971).

¹¹ Eschrich, W., *Planta*, **60**, 216 (1963).

BOOK REVIEWS

Human Performance

Decision and Stress. By D. E. Broadbent. Pp. xiv+522. (Academic: London and New York, March 1971.) £7.25.

THIS important book started as the first Paul M. Fitts Memorial Lectures, delivered to the University of Michigan in 1969. In book form it is far from the spoken word; it is a lengthy, technical and closely reasoned treatment of human performance and ability, in conditions chosen to illuminate theoretical issues.

The author covered some of the same ground in his earlier *Perception and Communication* (1958). The present book, *Decision and Stress*, takes the earlier as its starting point, discussing new experiments and examining the development of ideas on selective attention, stress, arousal and vigilance over the last 1.2 decades since the earlier book appeared. These topics might be discussed from several points of view; the chosen view is that of the experimental psychologist, concerned not so much with neurological accounts, or how information is physically stored and handled by brains but rather with "systems" types of description. In engineering terms, this corresponds to "block diagrams", without reference to specific components or circuits. Such engineering terms are employed as filter, retrieval, filtering, gating, parallel and serial processing, switching time, and many more. Engineering terms and concepts are used to describe psychological and behavioural phenomena—such as vigilance, arousal, decision and stress—although we may not see these at any rate in human form in machines. Some psychologists object to this approach, arguing that man is "reduced" to systems essentially non-human. Others, however, hold that pertinent experiments can be conceived and formulated in these terms, and that they give measures meaningful to man.

Some of the difficulties of providing an adequate theory of human behaviour are brought out with Broadbent's list (page 440) of "weaknesses" of his earlier position.

(i) Both noise and sleeplessness have their greatest harmful effect late in the work-period, and are thus similar in this respect. On the other hand, they tend to cancel each other out if applied together, and are thus opposite in that respect.

(ii) The personality dimension of extraversion interacts fairly consistently with time of day, as if it corresponds to a state of low arousal. On the other

hand, it does not behave consistently in relation to noise or sleeplessness.

(iii) Alcohol interacts with incentive in the way one might expect if it produced high arousal, rather than being a depressant.

These are important statements about skill, which cannot be discussed in the general terms of an engineering or computer model of behaviour without adding a great deal about the special characteristics of people and differences between people.

Some of the experiments described here are elegant, especially where selection of speech information is studied as a function of selective switching between the ears, between voices, languages, or message content. The author is a pioneer of much of this, and he is generous to those (Triesman, Moray) who have modified his earlier views by later experiment and argument. Psychology is still largely a matter of fashionable opinions, but here we find, perhaps for the first time, what appears to be a neutral and objective treatment. The author's work receives no more emphasis and is defended with no more fervour than the views of his disciples/critics. But we are so used to "goodies" and "baddies" in psychological discussion that it is a formidable task to assimilate these arguments. Or is this because psychology lacks accepted "paradigms" (in Kuhn's sense) for making sense of experiment and observation through generally held assumptions?

It is clear that theories adequate for even "simple" skills will have to involve far more than transfer-function statements between input (stimuli) and output (behaviour). This suggests the need for psychological measures in many psychological experiments, and a far greater insight into the brain's logical operations. One is led to questioning how adequate are the conceptual and experimental tools of psychology; but in any case, this book uses the limited tools to maximum effect and our understanding is considerably increased.

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Mathematical Fantasia

Mathematics Made Difficult. By Carl E. Linderholm. Pp. 207. (Wolfe: London, October 1971.) £2.75.

DR LINDERHOLM's book is far removed from the run-of-the-mill mathematics text. That it is confusing and lacking in structure does not, unfortunately, set it apart from all others; that its author

deliberately tries to confuse, and joyfully acknowledges this in his introduction, does. The book aims, then, not to expound, but to mystify, interest and amuse.

As the book claims, the reader is "coaxed deeper into the eerie landscape of central mathematics. Forgetful functors stare back at you between wild trees; arrows fly in all directions; your feet become entangled in an undergrowth of morphisms; your eyes behold the universally repelling object". In the cause of greater confusion, the reader is assumed to know what categories, functors, monoids, and so on, are, or to be sufficiently intrigued by what the author reveals about them to seek elucidation elsewhere. That mystification and interest can profitably precede enlightenment is well known to teachers, but is often forgotten by authors. So, too, is Dr Linderholm's method of asking a question and then disposing of various fallacious replies before revealing the answer.

To take this book as the excuse for a sermon on pedagogy would, however, be wrong. It is a *jeu d'esprit* that should be treated as such. True, it contains much involved and deep mathematics that demonstrate, in particular, how pure mathematicians now concentrate their attention on mappings rather than on the things on which they are defined. Thus a "modern" view is that "a group is a category with one object in which every morphism is an isomorphism".

Not all the book, though, is on this level. Quadratic and cubic equations, for example, are studied through a "real-life" example based on the tribulations of the baker of Beaulieu Derrière. There is an amusing section on the sex life of brackets, and the African travels of that famous journalist and explorer, Dr L. I. Presume (Livingstone to his friends), serve to introduce some topological notions.

The dust jacket compares this book with *Alice in Wonderland*. It is not a particularly apt comparison, for this work is far more mathematical. Indeed, comparison with this book and, say, Carroll's *A Tangled Tale* only emphasizes the gulf that now exists between the mathematics of the educated man-in-the-street and that of the professional. Can one expect the former to grapple with this book, to enjoy its in-jokes and in-puns? I fear not.

For the mathematician, and others prepared to follow some of the trails laid by Dr Linderholm, the book has much to offer. Friends who have seen it have all found something in it to amuse them—although their mathe-

mathematical backgrounds differ as much as their senses of humour. It is an engaging *mélange* of shaggy-dog stories, whimsy, facetiae and mathematics; a book to be dipped into, rather than read from cover to cover. One hopes, however, that a paperback edition will soon appear, for in its expensive, hard-back form the book might have disappointingly few readers. A. G. HOWSON

Uses of Far Infrared

Far-Infrared Spectroscopy. By K. D. Möller and W. G. Rothschild. Pp. xix+797. (Wiley: New York and London, June 1971.) £14.25.

THIS book is in the tradition of monographs on special aspects of optical spectroscopy exemplified by the classical works of Theodore Lyman on the vacuum ultraviolet and of Coblenz and Lecomte on the infrared spectrum. In the far infrared, defined as the range of wavelengths from 50 μm to 1 mm, black-body radiation from incandescent sources is several orders of magnitude less intense than in the near infrared. Absorption spectroscopy is correspondingly more difficult, and only since the early 1950s have new instruments and techniques enabled the ready exploitation of the region. In fact, according to the bibliography given in the present volume, in the past twenty years four times as many far infrared papers have been published as in the entire previous history of the subject. It is thus time for a monograph to review the status of the field, and the authors have provided a good one.

The first quarter of the text is devoted to instrumentation. Grating spectrometers, Fabry-Perot and Michelson interferometers, and auxiliary components—sources, detectors, multi-reflexion cells, filters and so on—are reviewed in satisfactory detail. The treatment of order-separating filters for grating spectrometers is particularly well done.

The main part of the book reviews applications of far infrared spectroscopy to physical chemistry and solid-state physics. Of interest to chemists are four chapters on low molecular frequencies due to heavy-atom vibrations, hydrogen-bonded complexes, and multiple potential minima, and three chapters on free and hindered molecular rotation in gases and condensed phases. The solid-state topics are introduced by two chapters on elementary theory and applications of the vibrational spectra of crystals. These are followed by five appendices on the far infrared spectroscopy of lattice impurities (written by A. J. Sievers), ferroelectric materials with the perovskite structure (C. H. Perry), magnetic phenomena (I. F. Silvera), semiconductors (R. Kaplan) and superconductors (G. K. Gaulé). In view

of the specialized nature of such topics, the preparation of the appendices by experts makes the treatment authoritative. The volume concludes with a brief appendix on rapid-scan Fourier-transform spectroscopy (E. V. Lowenstein) and a reproduction of the widely known far-infrared bibliography of E. D. Palik (1,512 entries from 1892 to 1969).

A serious flaw in the book is the omission of any treatment of laser studies in the far infrared. While it is true that tunable far infrared lasers are not yet widely used for spectroscopic purposes, their potential for high-resolution and high-speed spectroscopy is clearly indicated by work at shorter wavelengths. However, because of the rapidity with which the laser art is advancing, it is perhaps unfair to expect to find such material in the present volume. Though its copyright date is 1971, the last year covered in the bibliography is 1969, and the references at the end of the individual chapters contain few entries later than 1968.

Other topics where the book seems to me to fall short in completeness or scholarship are in the references to the older literature and in the subject of ring vibrations. The book quite rightly regards Rubens as the father of far infrared research, but the bibliography seems to include all of Rubens's papers, without regard to whether they have anything to do with the far infrared (for example, ref. 84 is a paper on the photoelectric effect in gold films). Conversely, other early contributors to the development of techniques that have become valuable in the far infrared are omitted. So far as I could see, the only reference to A. H. Pfund is a bibliography entry dealing with the Welsbach mantle as a source of far infrared radiation. His classical works on crystalline powders as selective radiators, on selenium-plate polarizers for the infrared, on the properties of blacks for detector surfaces, and especially on the resonance radiometer (the forerunner of narrow-band AC amplification) are missing entirely. R. W. Wood, the inventor of the echelette grating, rates only seven entries, and W. W. Coblenz none at all. The classical 1931 paper of Cleeton and Williams on the absorption of ammonia gas at 1.5 cm, the first to bridge the gap between radiofrequency and far infrared spectroscopy, is not cited.

The least satisfactory of the chemical chapters is that on the "Skeletal Modes of Strained Ring Systems". The choice of four-membered-ring molecules for discussion is poor and pseudorotation in five-membered rings is inadequately treated. The work of Durig and Wertz on cyclopentane, in which pseudorotation in that molecule was first shown spectroscopically, is not cited. All but one of the examples selected to illustrate the topic with spectral data are not in

fact true pseudorotators because the five-membered ring contains a double bond.

Apart from these minor points, the book is to be warmly recommended. It belongs on the shelves of science libraries and of serious workers in the field of infrared spectroscopy. Research workers in other areas will find it a good place to learn what the far infrared can offer to help them attack their own problems in molecular structure and solid-state physics. RICHARD C. LORD

Russian Fluid Mechanics

A History and Philosophy of Fluid-mechanics. By G. A. Tokaty. Pp. vii+241. (Foulis: Henley-on-Thames, April 1971.) £4.50.

ACCORDING to the jacket, in 1947 the author "became the Chief Rocket Scientist responsible to I. V. Stalin himself". According to the author (p. 155), "The history of science and technology is far from being free from misconceptions and the tyrannical influences of certain dogmas . . ."; fluid philosophy seems to consist in a dogma attributed to Bobylev (p. 127): "No man should ever undertake experimental investigations until and unless they are demanded by a 'solid theory'." Of course Russians must be given credit for a lot of things denied them by the dogmatic. The author attributes to Lomonosov (p. 121) the "outstandingly original" proof "both theoretically and experimentally" that gases are compressible, the concept that the "insensible particles" of bodies have "mass, weight, volume, colour, taste, etc.", on which "the whole continuity theory of fluid mechanics rests", and the invention of the helicopter (pp. 122–123). As evidence that "the secrets of the atmosphere captured Mendeleyev's imagination to such an extent that he soon became an organic part of the Russian school of fluid mechanic thought", the reader learns that (pp. 123–124) Mendeleyev "personally ascended in a balloon to an altitude of more than three kilometres". While the author lists the titles of eight of Ostrogradsky's papers on subjects other than fluid mechanics, he deprives his countryman Euler, despite heaping upon him more than his customary number of superlatives, of credit for several of his abundantly documented discoveries: the "Lagrangian description" (p. 78), the "Bernoulli equation" (pp. 79–80), the stagnation region ahead of and behind a blunt obstacle (p. 81), and the d'Alembert paradox (pp. 81–82).

This book should be rated strictly X for those who do not already understand the mechanics of fluids and know its history. For those who do, it may pander to the wicked habit of collecting howlers. Examples on fluid mechanics itself: "Experimentally . . . in actual fact, bodies of all weights fall from the

same height in the same time" (attributed to Galileo, p. 18); in vortex flow generated by a long cylinder spinning steadily in a viscous fluid, "the periodic times of the parts of the fluid are as their distances from the axis of the cylinder" (Newton's "proof" is quoted in full on pp. 68–70, with no mention of Stokes's correction); the viscosity of all fluids is a decreasing function of the temperature (p. 70); Borda flows are not "in harmony" with classical hydrodynamics (p. 83); Lagrange's velocity–potential theorem is "more general" than Helmholtz's theorems, and a potential flow is free of the "distortions implied by the Cauchy–Helmholtz theorem" (pp. 110–111); all three normal pressures in a Navier–Stokes fluid are equal ("a simple but important fact, which made Navier's task easier", p. 90), that task being to put the "buttons of viscosity" on the "beautiful trousers" tailored for hydrodynamics by Euler (p. 88).

Examples on the history of fluid mechanics: the work of d'Alembert, Euler, and Lagrange was limited to potential flow (p. 105), Laplace gave us "the mighty equation" of potential theory (p. 106), Lazare and Sadi Carnot were one person (pp. 101–104). Among interesting sidelights are the fact that Dante, whose importance in fluid mechanics has been overlooked until now, was "the last great poet of the Dark Ages" (p. 31), that Leonardo da Vinci wrote in misspelled modern German (p. 47), and that in 1890 Tsiolkovsky, "the acknowledged father of rocketry", arrived all by himself at the Newton–Euler impact theory "in a typically Tsiolkovsky manner" (p. 129). Some readers may find interesting the author's enthusiasm for rotor ships and his anecdotes about various engineers, mainly Russian and German, whom he has known. Just to keep our feet on the ground of real science, the author closes with the obligatory tribute to Einstein and "the universal matter–energy continuity." C. TRUESDELL

Molten Salts

Advances in Molten Salt Chemistry. Vol. 1. Edited by J. Braunstein, Gleb Mamantov and G. P. Smith. Pp. xii+284. (Plenum: London and New York, 1971.) £8.20.

MOLTEN salt chemistry may be judged to have "come of age" or at least achieved general recognition by the publication of the first volume of a series of "Advances". Greater appreciation of this most interesting, yet at present little known, field is certainly to be desired and the series is to be welcomed as a most useful step towards this aim.

The volume comprises five articles; that on vibrational spectroscopy by R. E. Hester will doubtless supersede the

well known review of this topic by D. W. James in Blanders's *Molten Salt Chemistry*. Y. Marcus gives a detailed account of liquid extraction from molten salts which should stimulate study of distribution coefficients for the many systems at present unexamined. C. R. Boston gives an interesting review of haloaluminate melts which occasionally digresses and suffers by making no mention of the numerous interesting low oxidation state species recently found by Bjerrum and Corbett with tellurium and selenium, G. P. Smith with titanium, and Mamantov with mercury. D. A. J. Swinkels follows with a more technologically orientated discussion of molten salt batteries and fuel cells which makes mention of economic factors and even devotes a few pages to solid electrolyte cells. The volume concludes with a treatment of the somewhat specialized topic of the mass spectroscopy of molten mixed halide systems by J. W. Hastie.

These reviews raise the not uncommon problem of how far it is desirable to recapitulate a necessarily brief and unrigorous account of theory and experimental procedures, very similar to those which have appeared in earlier reviews. With the advent of a regular series, however, it should be possible to achieve a decrease in size and cost of future volumes by including references to earlier articles.

Since all these articles are concerned with areas in which other reviews have been published 2 to 7 years earlier, some repetition has occurred, accentuated by the inevitable time lag of publication (hardly any references, except those of the authors, are dated 1970). Whilst some updating of reviews is clearly necessary it is to be hoped that the editors will be courageous and deal with less familiar areas in later volumes, such as the reaction chemistry of specific melts, for example acetates or thiocyanates, the vexed question of the acidic–basic species in molten nitrates, or the industrially important borate, phosphate and silicate melts.

Purists must be warned that they may wince at certain colloquialisms, such as "free Li sloshing around". There is also a fair number of misprints (fortunately mostly not serious) with the heaviest concentration in Chapter 2. The indexes seem good, but the binding is rather flimsy for a work of reference.

All practitioners of molten salt chemistry, and also those interested, will need to regard this series of reviews as obligatory reading, at least until the creation of a primary journal devoted to this branch of chemistry, for at present original papers are necessarily scattered through a considerable range of journals and therefore not fully appreciated by workers on other aspects of the field. D. H. KERRIDGE

Chimpanzee Sociology

In the Shadow of Man. By Jane van Lawick-Goodall. Pp. 256. (Collins: London, October 1971.) £2.50.

THIS book tells the story of a remarkable research project; it is written in popular terms and has been widely reviewed in the daily press. In spite of its popular nature, the account which Dr van Lawick-Goodall presents here of the chimpanzees at the Gombe Stream National Park, Tanzania, is of considerable scientific interest. She has already presented a detailed scientific account of much of her work in a monograph published in 1968, and that account is of great value to the specialist in the field of animal, and particularly of primate, behaviour. It is, however, a relatively formidable document for the non-specialist, and there must be many who, while not inclined to tackle the wealth of detail in the earlier report, are interested in obtaining a general account of the author's chimpanzee work. This book answers just such a need. Written in an easy, chatty style, and illustrated with magnificent photographs taken by her husband, Hugo van Lawick, it tells of the author's first visit to Gombe in 1960, of her early difficulties in getting close enough to the chimpanzees to observe them, of her later successes and more recently of the setting up of a research station manned by several research students.

The fact that the author carried out her work under such conditions of isolation and over such a long period of time is a tribute to her persistence. The result of this persistence is one of the most detailed longitudinal descriptions of a primate's behaviour yet produced. While not presenting the detailed data from which the author draws her conclusions, the book contains the main features of chimp life which she discovered. It describes the social organization of the chimp group, with its relatively loose knit structure and with the dominance hierarchy and complicated dominance relationships that exist between adult males. Perhaps, though, the most valuable feature of this book is the way in which it describes the chimps as individuals, each with its own quirks of behaviour. At first this individuality is a little difficult to stomach. One comes across descriptions of behaviour involving Flo, Mr McGregor or Leakey and one wonders if one is leaving the world of objective observation and entering that of Beatrix Potter. But the feeling soon disappears. In one of the key sentences early in her book, the author writes that she is interested in the differences between individuals as much as anything else, and the subsequent pages show just how greatly the individuals of the groups do differ in their behaviour.

This is, of course, something which has been recognized in other primate studies; indeed the very idea of dominance stems from this assumption. Probably, though, no other study has shown in quite so much detail how individuals do differ, not only in dominance, but in sexual behaviour, methods of child care and less easily definable qualities such as intelligence and inventiveness.

The book contains descriptions of many different aspects of behaviour of great importance; topics such as meat-eating, tool-making and tool-using and infant care are each dealt with in detail. Perhaps one of the most immediately striking of the observations made in the book concerns the decisive effect which loss of the mother can have on her infant's development, a feature which has also been found in laboratory studies on rhesus monkeys, and in children who have been deprived of adequate mothering.

In short, the book is an admirable popular summary of Dr van Lawick-Goodall's work at Gombe and presents in easily digestible form many observations of great importance.

N. R. CHALMERS

Pheromones

Communication by Chemical Signals. Edited by James W. Johnston jun., David G. Moulton and Amos Turk. Pp. x+412. (Appleton Century Crofts: New York, 1971.)

WHEN does a chemical become a signal? This first volume of the series "Advances in Chemoreception" sets out to establish the circumstances. The answer seems to be—when it initiates a behavioural response in an individual or a population and, in the present context, when it is produced by another animal. The involvement of odours in inducing or modifying behaviour has long been familiar. The physiological basis has only been studied with any vigour since advances in chemical technology enabled the chemical composition of microgram quantities of the relevant biological materials to be established. The tool is the gas chromatograph combined more recently with the mass spectrograph. This book gives a very comprehensive account of those chemicals which are secreted to the exterior of one individual and which are detected by another individual of the same species in which they release a specific reaction, especially in invertebrates. The term "pheromone" was coined in 1959 for such chemicals and within a decade had both codified and released a flood of information. Pheromones can now be identified as determining not only the behaviour of individuals but, in social insects, of the whole colony; for example, cohesion in

a honey bee swarm is dependent on a pheromone (9-hydroxy-trans-2-decenoic acid) produced, among at least twenty others, by the mandibular gland of the queen. The sites of origin of pheromones have frequently yielded identified chemicals, and electrophysiological studies are now yielding precise information about the location and characteristics of the receptor sites in the receiving organisms. The pheromones may act in very low concentrations, via the nervous system, on the endocrine system and thus modify reproductive activity; these are the "primer" pheromones. Others may, again via the central nervous system, elicit immediate behavioural responses—the "releaser" or "signalling" pheromones.

The more stereotyped behaviour of insects has made them easier to study than vertebrates and, in addition, the chemical signal is often a single chemical or comprises a small group of chemicals all of small molecular weight. In mammals, fish and reptiles which have an array of senses, more complex central nervous systems and greater flexibility of behaviour, the pheromones are not only more difficult to study, though of considerable importance, but may also be much more complex and individually specific mixtures of chemicals, although the individual chemicals may still be of low molecular weight.

There is no doubt, however, both of the present richness of the field, especially in invertebrates, and the potential importance of chemical signals for a better understanding of behavioural activity. Both aspects are richly documented in this book which clearly establishes the role of chemical signals in communication. A. IGGO

Electrochemistry

Reactions of Molecules at Electrodes. Edited by N. S. Hush. Pp. xiv+498. (Wiley: New York and Chichester, September 1971.) £9.50.

"THE study of electrode processes occurring at a metal, semiconductor or insulator interface forms an important part of electrochemistry" (N. S. Hush). This volume is an attempt to describe some basic aspects of modern electrochemistry in a form suitable not only for the electrochemist but for research workers in other fields. The proliferation of reviews in electrochemistry of recent years, mostly of a specialist nature, has not helped to widen the basis of the subject. The nine articles in this volume attempt to bridge this gap. The importance of the subject matter may be judged from the large contribution to this volume from the Russian school.

Much of this book is concerned with organic systems, so it is fitting that the first chapter should be by A. N. Frumkin from whose works much of modern

electrochemistry derives. In collaboration with B. B. Damaskin, he presents a clear critical description of the theory of the adsorption of organic molecules at a wide variety of electrodes. The bibliography is representative and clearly shows the strength of the Russian school.

The role of the solvent, an aspect of the electrochemical system all too infrequently discussed, is emphasized by the inclusion of an admirable discussion of ion solvation by B. Case. The author discusses the problems of solvation in aqueous solution, alcohols and alcohol water mixtures, the amides and aprotic solvents relating the latter systems to their aqueous analogues. Many of the most useful electrosynthetic processes probably occur in aprotic solvents, and the paucity of reliable thermodynamic data for these media is again emphasized.

The theoretical aspects of electrode processes are described by R. R. Doganadze in terms of the quantum theory. By presenting a general description as far as possible, he achieves remarkable clarity. Of special interest is the detailed discussion of the transfer coefficient α . The problems of the model for electron transfer in systems where ionic solvation predominates are discussed by J. M. Hale. Although the distinction is occasionally artificial, internal and external energies of rearrangement in forming the transition state of these systems have been calculated for their reductions at metal electrodes. Except for brief treatment by Doganadze, the only electrode material to be treated in detail is the intrinsic organic semiconductor by W. Mehl. The theory and practice of interfacial reactions at aromatic hydrocarbon electrodes where the donor and acceptor are a redox system in solution are discussed. The treatment is extended to photoexcitation of both the electrode and redox species.

In an article requiring extensive electrochemical knowledge, M. E. Peover relates the electrochemistry of aromatic hydrocarbons to theoretical considerations. B. J. Tabner and J. R. Yandle attempt to relate the electrochemical characteristics of aza-heteromolecules to orbital energies on the basis of an oversimplified model. In a section directed towards the inorganic chemist, J. A. McCleverty describes transition metal complexes of dithiolene and organo-metallic compounds.

The section by M. Fleischmann and D. Pletcher should have wide appeal, for the authors have assembled a "pocket book guide" to organic electrosynthesis, avoiding excessive referencing and concentrating on functional group reactions, some useful synthetic reactions and cyclization reactions.

This book must be recommended, although it is debatable whether at times it remains entirely within the bounds of its initial concept. R. M. REEVES